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# CONGENITAL HYPERTROPHY OF THE MUSCLES, EXTRAPYRAMIDAL MOTOR DISTURBANCES AND MENTAL DEFICIENCY

## A CLINICAL ENTITY

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Within a relatively short period three infants of unrelated families were admitted to the Children's Clinic of the University of Amsterdam, all of whom presented congenital hypertrophy of the muscles, extrapyramidal motor disturbances and mental deficiency. The report of a fourth case was found in the literature. After the death of the first child, examination of the brain was possible.

### REPORT OF CASES

CASE 1.—A boy, born on Aug. 17, 1930, in a village in the province of North Holland, was the eleventh child of healthy parents. There had been three miscarriages between the normal births. Six of the children had died; two of these were stillborn, and one of the latter had a congenital cerebral anomaly (anencephaly?). One child died at the age of 8 months following intussusception of the intestine; one lived for only five days, and one died of convulsions at the age of 6 months. The tenth child reached the age of 9 weeks. According to the mother, this child had symptoms similar to those which I shall presently describe. It became rigid and perspired profusely, and the head was bent at the neck. One of the mother's brothers had a child suffering from spina bifida.

The eleventh child was born spontaneously and weighed about 4,000 Gm. He cried immediately after birth and was not cyanotic. The mother was impressed by the fact that the child's throat was short and broad and that the pectoral muscles were massive. She remarked on these symptoms on the first day. The child was hypertonic at birth. The nurse told the mother that his hands grasped her fingers much more tightly than those of other new-born children. Breast feeding was difficult. At auditory stimuli the child shrank and the limbs were convulsed. The same movements occurred if one stroked the child's face. These reactions were so exaggerated that they may be compared with those in the premature infant. The rigidity increased, and the head was still more bent at the neck. Sleep was restless, and the infant often moaned; he seemed mentally backward. At the age of 2 months he was sent by the house physician to the outpatient department and thence was admitted to the clinic.

The weight on admission was 4,390 Gm. The child looked strange. The skull was asymmetrical; the sutures were closed and perceptible to the touch as ridges. The occiput protruded; the parietal bones lay beneath the occipital bones in the

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lambdoid suture. The index cephalicus was 69 cm.; the greatest circumference of the head was 36.5 cm. The skin over the cranium was loose and could be folded. The ears were large, unwieldy and thick. The right eyeslit was somewhat wider than the left. The pupils were equal in size and reacted to light. Most of the time there was a slight rotation of the head to the right, and opisthotonos was as pronounced as in protracted epidemic cerebrospinal meningitis. This severe opisthotonos disappeared when the child was held by its feet for a moment.

Fig. 1 (case 1).—Front and back views, showing muscular hypertrophy, hypertonia and rigidity, with the head bent backward at the neck.

Fig. 2 (case 1).—Lateral view.

The legs were vigorously extended every now and then; they were often crossed. The knee reflex jerk was present, but the achilles reflex was absent. The legs were not paralyzed; every movement could be made. The tonus varied greatly; this was seen especially in the feet. The arms were bent at the elbows, and the hands at the wrists; the rigidly bent fingers caused a lesion of the vola manus by their continual pressure. If the arms were passively extended, they sprang back in the fashion of a claspknife, but if a certain angle was reached the rigidity suddenly gave way. Paralysis was absent. There were marked hyper-

trophy of the flexors of the arms, especially of the brachioradiales, less marked hypertrophy of the pectorales majores, deltoidei, trapezii and obliqui abdominis, and a moderate degree of hypertrophy of the quadriceps femoris and the triceps surae on both sides. The muscles were hard to the touch. The hypertrophy was symmetrical (figs. 1 and 2). There was also so-called stridor laryngis inspiratorius congenitus benignus.

On first examination the urine contained a rather large amount of albumin, without cells or casts; on second examination no albumin was found. A roentgenogram of the skull revealed no further abnormalities. The Pirquet reaction and the Wassermann reaction of the blood were negative. The fundi oculorum were normal. The child had no fever except on one day. He stayed in the clinic from October 24 to November 1, and died at home on December 19. According to the mother, the rigidity became worse.

Postmortem examination was made by Dr. E. Hammer, pathologist of the Binnengasthuis at Amsterdam.

CASE 2.—A boy, born on April 3, 1931, was the only child of parents no longer young. There had been no miscarriages. The child was premature. The weight was 1,800 Gm. at birth; at the time of admission to the clinic, on June 2, it was 3,340 Gm. During the first two weeks of life the patient was breast fed; after that he was given buttermilk, on which he flourished. During the first weeks micturition was difficult; therefore the prepuce was loosened from the glans penis. Before this was done the skin over the mons pubis was found to be hard and thick; this condition had become more marked during the last weeks before admission. On first examination in our outpatient department the child still showed this change; also, the skin over the front part of the thighs had thickened and hardened. These changes gradually disappeared during the child's stay in the clinic; they were diagnosed as sclerema or edema durum. The mother stated that the child was not particularly fretful but that he continually made movements of extension, stretching and pressing.

At first sight we were impressed by the appearance of the child, which may best be compared with that of a wrestler or athlete. There were a short, broad throat and neck, broad shoulders and symmetrical hypertrophy of almost every muscle, which was most marked in the biceps, brachioradialis, quadriceps femoris and triceps surae. The muscles were as hard as stone. The arms were hypertonic; every now and then they were rigidly extended or flexed, and it was difficult to alter the flexion passively. The legs were rigidly extended most of the time. Paralysis was absent. The head was bent backward. If one moved the lower jaw to inspect the mouth, clonus of the jaw occurred. The child was so hypertonic that he was able to stand upright with only a slight support at the back of the head.

The knee jerk reflex was lively; the achilles reflex could not be elicited.

The skull looked normal; the fontanel measured 2.5 by 2 cm., and when its borders were pressed down they sprang up again. There was craniotabes along the lambdoid suture. The child had a vigorous voice. The heart and lungs were normal. The recti abdominis were hypertonic. The liver and spleen were not enlarged. Examination of the blood showed: 64 per cent hemoglobin (Sahli), 3,100,000 red corpuscles and 6,000 white corpuscles. A differential count gave: polymorphonuclear neutrophils, 14 per cent; eosinophils, 4 per cent; basophils, 1 per cent; lymphocytes, 77 per cent, and monocytes, 4 per cent. There were slight anisocytosis and poikilocytosis. Three nucleated erythrocytes were found to

one hundred leukocytes. The urine contained a trace of albumin, and some red and white blood corpuscles were found in the sediment. The temperature was normal during the first two weeks, with an exception of one rise to 38.2 C. (100.7 F.); afterward it was somewhat subnormal. Notwithstanding the fact that the patient was fed on breast milk, he was wasting away and came to have the appearance of a child in a state of decomposition (Finkelstein). The bowels were loose. The child collapsed during the night of June 23 and died in the morning.

Postmortem examination was performed by Dr. E. Hammer. Section of the head was forbidden. Dilatation of the heart, especially on the right side, was observed. There were bronchitis, bronchiolitis mucopurulenta and slight fatty degeneration of the liver. The spleen resembled that found in patients with infections. The intestine showed marked hyperplasia of the lymphoid system, necrosis and ulcers originating from the plaques and follicles of the ileum and colon. Some lymphocytes were observed in the glomeruli of the kidneys and within Bowman's capsule.

CASE 3.—A Jewish boy, born on Aug. 29, 1932, was admitted to the clinic on December 23. The mother had previously given birth to healthy twins.

The child was born spontaneously at term; he became icteric the second day of life. The icterus was marked, and he was dull and apathetic. Immediately after birth the backward position of the head was noted. During the following months the child gave the impression of being mentally defective, but according to the mother he later followed a moving object with his eyes.

On admission, the weight of the child was 4,600 Gm., and the height 54 cm. He always assumed a lateral position. When he was placed on his back, he kept an *arc de cercle* attitude for some moments, but soon resumed his former position. The head was bent backward to such a degree that the occiput was almost in contact with the back. The greatest circumference of the head was 40 cm.; the index cephalicus was 79 cm. The fontanel was somewhat sunken; the borders were firm, and the dimensions were 3.5 by 3 cm. The mouth was large, and the tongue was large and thick. A real frenulum linguae was lacking, the tongue being attached to the bottom of the mouth with a very broad base. The roof of the mouth was high. The bridge of the nose was somewhat broad and sunken, and the nostrils were widely open. The border of the hair was low; the hair was fine and sparse. The pupils reacted somewhat sluggishly to light. The child did not attend to his surroundings; therefore, it is not possible to state whether the pupils reacted in convergence.

The cranial nerves were intact.

The ears were large, flat and unwieldy and closely resembled those of patient 1. A roentgenogram of the skull revealed no further abnormalities. Facial mimicry was reduced; the voice was heavy, like that of an infant with myxedema congenitum. Crying began and ended slowly. It may be compared to the sound of a swelling and dying siren. Sometimes the child cried for a long time without apparent cause. To a certain extent, he seemed to like a ventral position.

The throat was short and broad, with two transverse folds. The heart and lungs were normal; the liver and spleen were not enlarged, and the urine was free from albumin and sugar. No increased pressure was found on lumbar puncture, and the spinal fluid was chemically and microscopically normal. The Sachs-Georgi test gave negative results for the spinal fluid; the Wassermann reaction of the blood was also negative.

In the sacral region slight hypertrichosis was present.

The muscular hypertrophy caused an odd appearance. The hypertrophy was most marked in the deltoideus and triceps surae, but the pectoralis major, biceps, infraspinatus, quadriceps extensor femoris and obliquus abdominis externus were also hypertrophied and were hard to the touch. One had the impression that all the skeletal muscles were involved in the process. In this case also the appearance was that of a small athlete or wrestler (figs. 3, 4, 5 and 6).

Most of the time there was pronounced hypertonia. With only a slight support at the head, the child was able to stand upright. In general, it was possible to

Fig. 3 (case 3).—Characteristic muscular hypertrophy.

Fig. 4 (case 3).—Legs and feet of patient, showing muscular hypertrophy and rigidity.

bring the chin in contact with the breast without great effort, but every now and then the resistance was more powerful. The head always resumed its former position immediately, if left to itself. Passive lateral movements of the head could be made with ease. All active and passive movements were possible; there was no paralysis. The child did not make any unvoluntary rhythmic motion. Movements were few and slow. In crying, he did not move the arms and legs like other children of this age.

The arms were continually flexed at the elbows and usually not at the wrists; the fingers were generally flexed at the metacarpophalangeal joints. The fingers

themselves were alternately extended and flexed. The tonus of the arms varied greatly. One moment they were markedly hypertonic; the next moment their tonus was normal, or they might be flaccid. The same held true for the legs, although most of the time they were hypertonic. There was no so-called clasp-knife rigidity. The reflexes of the arms were present, but were not exaggerated. The legs were sometimes extended, at other times flexed. The knee jerk reflex was sometimes lively; at other times it was difficult to obtain. The achilles reflex was generally present. In looking for Babinski's reflex, one did not see a dorsal flexion of the great toe, but there was spreading of the other toes. Now

Fig. 5 (case 3).—Appearance of patient in the ventral position.

Fig. 6 (case 3).—Appearance of patient in the habitual lateral position.

and then there was spasm of the adductors. When the child was grasped at the armpits and held upright the legs did not cross.

The abdominal reflexes were not constant.

During the following days of the infant's stay at the hospital it was possible to obtain further particulars. During sleep the head was bent backward to a lesser degree than when he was awake. When sleeping he often produced a snoring sound; when awake he babbled. If one awakened him by letting down part of the bedstead, myoclonic movements of the arms and legs occurred, the head became more bent at the neck, and he made grimaces and babbled. When he became excited the tonus increased. After some moments it lessened, and the joints became wholly relaxed. If the child was held up sideways, he extended the

lower arm and flexed the upper one, but the head did not turn with the chin downward, as in normal infants. He kept the head backward in the medial line. If the examiner turned the child's head to the lower shoulder, the lower arm was vigorously extended, and the upper arm was flexed.

When the head was turned while the child was in a recumbent postion, one saw extension of the arm in the so-called jaw-arm reflex and raising of the arm in the so-called skull-arm reflex (positive Magnus-de Kleyn reflexes). The legs did not participate in the Magnus-de Kleyn reflexes, as is the case with normal infants.

If the child was poised in mid-air in a ventral position, the head dropped, and the arms and legs were slightly flexed; then he tried to extend the legs, and the pelvis was raised. When the examiner pressed his hand slightly against the soles, the child made a movement of creeping on the belly, using the hand to propel himself. When he lay in a ventral position with eyes open, he wrinkled his forehead.

The bulbi oculorum moved coordinately, but downward rotation was a little exaggerated; therefore, more white of the upper part of the eyeballs showed than is normally the case. If the child was in a vertical position and was turned round his longitudinal axis, rotatory nystagmus and after-nystagmus occurred. The menacing reflex was lacking, which is normal in children of his age. While he was in a ventral position, the eyeballs did not turn upward.[1] On pinprick he swiftly withdrew the arms and legs and began to cry. The functions of the bladder and the rectum were intact. The facial expression did not undergo any change if a small quantity of fluid with an acid, sweet or salty taste was put into his mouth. In testing some of the hypertrophied muscles with the galvanic current, the reactions were normal.

On Jan. 20, 1933, he was discharged from the hospital, but afterward was brought to the outpatient department several times. There were no perceptible changes in his status or behavior. On March 16 he was readmitted to the clinic in a deplorable state, with bilateral pneumonia, and died the night after admission. Postmortem examination was not permitted.

On studying the literature on this subject I found only one case recorded, which, however, is interesting. This was reported by Franz Bruck:[2]

Surgical aid was sought for a girl, aged 10 months, because of a large tongue which impeded respiration and deglutition. As a therapeutic measure, two pieces were cut from the tongue, but the child was not examined further. After six months the tongue had again enlarged, and the difficulties returned. A complete examination was made. The muscular hypertrophy gave the child the appearance of an athlete or wrestler (fig. 7). The muscles with the most marked hypertrophy were the deltoideus, biceps brachii, triceps surae, flexors and outward rotators of the thigh, rectus abdominis, longissimus dorsi and muscles of the chin. Moreover,

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1. Dr. A. G. Schoo (thesis, Amsterdam, 1933), investigating criteria in the neurologic examination of infants, found upward turning of the eyeballs in four children suffering from cerebral abnormality.

2. Bruck, Franz: Ueber einen Fall von congenitaler Makroglossie combiniert mit allgemeiner wahrer Muskelhypertrophie, Deutsche med. Wchnschr. **15**:229, 1889. In the article one reads that the drawings were made after nature with the aid of photographs. They resemble primitive art somewhat, but yet give a good impression of the child's peculiar appearance.

there were pronounced spasms in the muscles of the extremities, especially in the deltoideus and outward rotators of the upper part of the arm, in the muscles on the lateral side of the pelvis and in those of the thighs and the calves. The muscles of the neck were also in a state of contraction. The child's head was continually bent backward, and the elbows were slightly flexed.

The upper extremities were short. One could not state with certainty to what degree active moments in the joints were possible. The marked resistance felt on moving the articulations could be conquered only forcibly, especially in the elbows: "War es gelungen, so bemerkte man, am besten am Biceps, wie die vorher gespannten Muskeln plötzlich in Erschlaffung übergingen." (After it had been done, one could notice, particularly in the biceps, how the previously tense

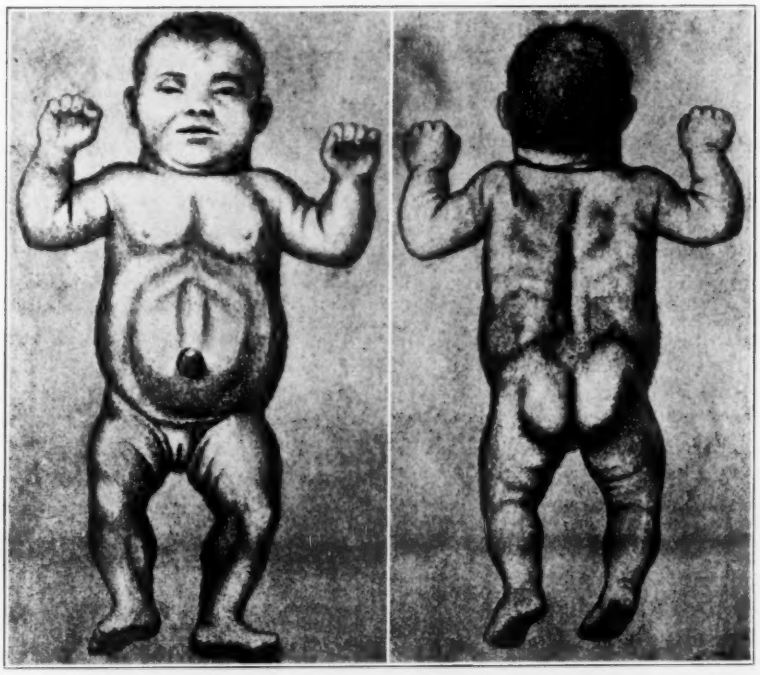

Fig. 7.—Peculiar appearance of a child with muscular hypertrophy (after Bruck).

muscles suddenly became relaxed.) These words are of great interest, as they are indicative of the extrapyramidal nature of the disturbances.

The mechanical excitability of the muscles and nerve trunks and the cutaneous reflexes had not increased. The knee jerk reflex was lively. No ankle clonus or knee clonus was present. The biceps reflex was lively, the triceps reflex less so. Auditory, gustatory and olfactory reactions seemed absent. The sensation of pain had somewhat diminished. On testing the muscles with the electric (galvanic and faradic) current, normal reactions were seen.

Microscopic examination of the pieces cut from the tongue and the deltoideus proved the existence of muscular hypertrophy. The child died of pneumonia at the age of 19 months. The postmortem observations will be discussed later in this article.

In the four cases described there was muscular hypertrophy of the nature of a congenital deformity. The coincidence of hypertrophy of the muscles and the bones in a monolateral, hemilateral and contralateral form is well known. Also, half of the face may participate. Other congenital deformities are repeatedly found, as, for instance, in Arnheim's [3] patient, in whom there existed, besides hypertrophy of the whole right side of the body, several telangiectasias, a large nevus pilosus in the sacral region and a cystic lung on both sides.

The athlete or wrestler habitus with the perfectly symmetrical muscular hypertrophy of the greater part, perhaps of the whole, of the skeletal muscular apparatus either is rare or else has not been described in medical literature. Kitaigorodskaja,[4] who treated the subject "angeborene Hypertrophie im Kindesalter" (congenital hypertrophy of childhood) extensively and who reported no fewer than fifteen cases of his own (hemihypertrophy, hypertrophy of one extremity, contralateral gigantism and hypertrophy of some parts of the body), did not mention any case of the athlete type. In one of his reports the only hypertrophy mentioned is that of the tongue. Evidently Bruck's interesting report did not come to his notice.

One might think that muscular hypertrophy is the result of constant and exaggerated contractions (*Arbeitshypertrophie*) of the muscles, which occur in utero. In this way some authors explain a hypertrophic pylorus in infants. This interpretation, however, is highly improbable with regard to the large tongue in Bruck's patient and in my patient 3. The presence at birth of hypertrophy also excludes its origin as contractions of postfetal life. Finally, it is well known that true hypertrophy may be preceded by myositis, phlebitis or neuritis. This etiology must also be discarded in the cases reported in this article.

Besides muscular hypertrophy, the extrapyramidal motor disturbances are predominant in the clinical picture. It is of interest that the punctilious observation of Bruck in 1889, at a time when these disturbances were not yet diagnosed, has made it possible to recognize them in the history of his case. The presence of extrapyramidal disturbances does not exclude other anomalies of the brain, but in connection with congenital muscular hypertrophy (so-called plus deformities) one's mind is fixed on a congenital pathologic process of the myotatic system, as will be discussed later in this article.

## PATHOLOGIC ANATOMY

Before stating the results of my own investigation, I shall give a brief résumé of the observations in Bruck's case.

3. Arnheim: Virchows Arch. f. path. Anat. **154**:300, 1898.
4. Kitaigorodskaja, O. D.: Jahrb. f. Kinderh. **125**:38, 1929.

The diagnosis of true hypertrophy of the muscles, made during life, was confirmed after death. Marked hypertrophy of the skeletal muscles was observed; only the glutei were somewhat thin. Moreover, there was hypertrophy of the wall of the intestine. The bowel had a large lumen. Also, the wall of the esophagus was somewhat thickened. The heart was small, without any hypertrophy.

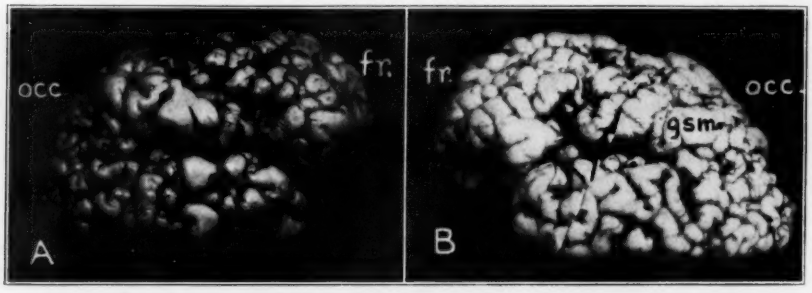


Fig. 8 (case 1).—*A* indicates the right, and *B* the left, side of the brain, showing asymmetry and polygyria; *fr.* indicates the frontal lobe; *occ.*, the occipital lobe, and *gsm.*, the gyrus supramarginalis.

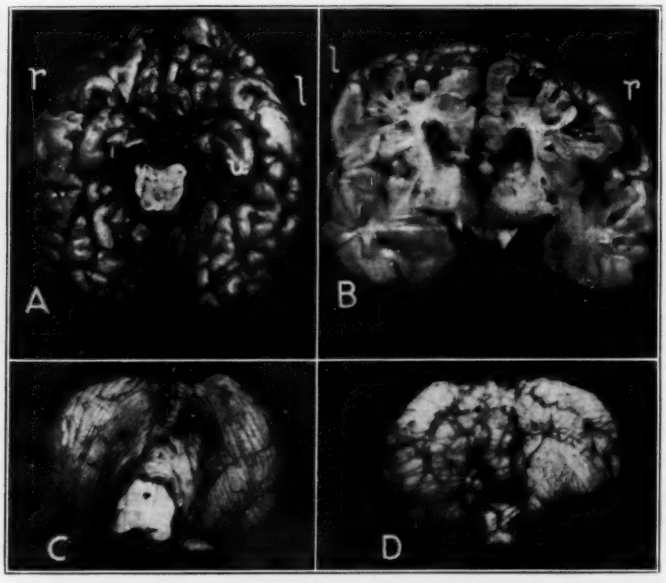


Fig. 9 (case 1).—*A* shows the right (*r*) and left (*l*) lobe, with the highly developed uncus (*u*); *B*, slight distention of the lateral ventricles; *C*, distention of the aquaeductus Sylvii, and *D*, the large vermis.

The brain and medulla spinalis were normal on macroscopic examination; only the gyri proved to be somewhat defective. As for the microscopic investigation, it is only stated: "die mikroskopische Untersuchung, besonders des Rückenmarks, zeigte nichts Pathologisches" (the microscopic investigation, especially of the

spinal cord, did not reveal anything pathologic). It seems highly probable that only a superficial examination of the brain was made.

*Observations in Case 1.*—The liver, spleen and kidneys were normal on microscopic examination.

The brain weighed 288 Gm. after having been in a solution of formaldehyde for some days. On section there proved to be hydrocephalus externus. Figure 8 shows the microgyria, which was most marked in the occipital lobes, more so on the left side than on the right. The frontal and temporal lobes were better developed than the occipital lobes. The base of the brain looked practically normal, but the pons was small, and the olives and pyramids were somewhat flattened. The gyrus supramarginalis (fig. 8 *B*) and the uncus (fig. 9 *A*) were markedly developed on both sides. The same was true of the gyri hippocampi. The insula lay free on both sides. Such an extensive polygyria and microgyria existed in both hemispheres that the topography of the different sulci could not be determined with certainty. In both the frontal and the temporal lobes longitudinal fissures were visible, permitting identification with normal conditions to a certain degree. The fissure of Rolando could be recognized in both hemispheres and indented the mesial side. The ventral parts of the gyri centrales posteriores were broad.

After the pons, bulb and cerebellum were removed by cutting through the pedes pedunculi, a frontal section of the brain was made through the middle of the third ventricle. The corpus callosum was thin, and the fornices were hypertrophied. There was a slight distention of the lateral ventricles. The centrum semiovale Vieussenii was poorly developed. In many places in the cortex, the centrum semiovale and the striatum small holes were visible. It was not possible to differentiate macroscopically between the putamen and the globus pallidus (fig. 9 *B*). The next frontal section was made through the frontal part of the septum pellucidum; here marked hydrops septi appeared. Another frontal section was made through the posterior part of the pulvinar and the roof of the mesencephalon, and the last section divided the occipital poles from the rest of the occipital lobes. The latter were united by the thin splenium corporis callosi.

The aquaeductus Sylvii proved to be wide. The lobi ansiformes cerebelli were small; the vermis and the flocculi, on the other hand, were well developed (fig. 9 *C* and *D*).

Numerous parts of the cortex of the cerebrum and cerebellum were embedded in paraffin, and the sections were stained with hematoxylin and eosin, toluidine blue, cresyl violet and Alzheimer's A and B stains. Moreover, frozen sections were stained with hematoxylin and sudan III. A part of the striatum was taken from the left side of the brain, embedded in pyroxylin (celloidin) and stained by the Nissl method. Finally, the different parts into which the brain had been divided by frontal sections were put into Müller's solution,[4a] embedded in pyroxylin and cut into serial sections measuring from 30 to 35 microns and stained by the Weigert-Pal or van Gieson method.

Cortex: The gyrus temporalis I, gyrus centralis anterior dexter, gyrus centralis posterior sinister, gyri frontales I and II, gyrus supramarginalis, uncus, gyri occipitales, cortex of the neocerebellum on both sides and the monticulus were examined microscopically.

Regarding the cortex of the cerebellum, only slight changes could be seen; in different parts of the sections the Purkinje cells were somewhat sparse and the tigroid substance had not an entirely normal aspect. The external granular layer

4a. Müller's solution has the formula: potassium bichromate, 2.5 Gm.; sodium sulphate, 1 Gm.; water, to make 100 cc.

was still present in most parts, which fact is in accordance with the age of the child. In the monticulus the Purkinje cells looked normal.

On the other hand, the cortex cerebri was ravaged by an extensive porencephalic process, localized for the greater part in the medulla corticis, but also in the layers of the cortex itself and on the border of the cortex and the medulla. The third frontal gyrus and the uncus were least affected. In the external granular layer of the uncus ganglion cells (Cajal-Retzius cells) were present.

The porencephalic process was not limited to the cortex and the medulla corticis (*Rindenblasenporencephalie*), but had spread through the whole brain,

Fig. 10 (case 1).—Occipital cortex; *a*, *a'* and *a''* indicate cavities (*Trümmerzone*); *b*, rarefaction (*Lückenzone*); *c*, status spongiosus, and *d*, a deep sulcus, with blood vessels and a large number of *Transportzellen* in the pia; paraffin section; hematoxylin-eosin stain.

producing everywhere the same histologic pictures. A large number of cavities were present, some of which were visible to the naked eye, while others were of somewhat smaller dimensions. A number of them, probably the older ones, were empty and lined with so-called *Körnchenzellen.* Cells resembling endothelial cells were also present, and in some spots the beginning of a membrana gliae limitans accessoria could be seen (figs. 10 and 11).

Another part of these cavities was filled with a fluid that stained an even red with eosin, and the whole wall was thickly lined with *Körnchenzellen.* Other

cavities contained a large mass of these cells and were even choked by them. In sections stained by the van Gieson method one could detect small red strings in these masses, which must be looked on as the beginning of an organizing process. However, I did not observe cavities that were totally filled with glial tissue (*Glianarben*).

In the nomenclature of Spatz, the cavities are called *Trümmerzone* (zone of débris). Next, the zone of cavities (*Lückenzone*) showed in my material as a rete of tender glial fibers in which *Körnchenzellen* were embedded. There were also

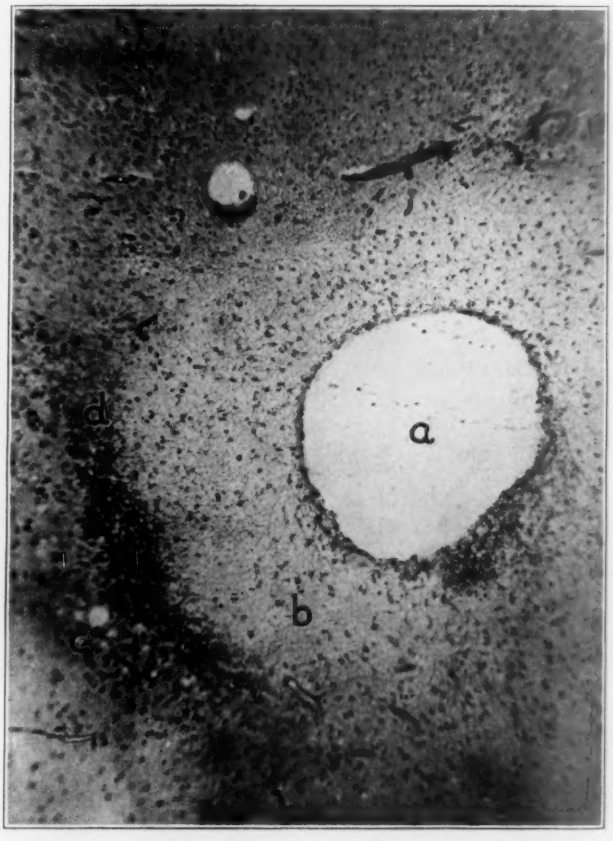


Fig. 11 (case 1).—Photomicrograph indicating: *a*, the cavity shown in figure 10, the wall of which is bordered with *Körnchenzellen*, which are at some distance from the porus, especially on the right (*Trümmerzone*); *b*, rete with sparse, large glial cells (*monströse Glia, Lückenzone*); *c*, status spongiosus, and *d*, hypertrophied glia; same staining as in figure 10.

large glial cells, often with a bizarre appearance and large processes (*monströse Glia*), glial cells with two nuclei, glial cells with phagocytosis and astrocytes with fibrils resting on a blood vessel. I could not detect any *Körnchenzellen* in the His-Robin spaces. In the zone of cavities (*Lückenzone*) every ganglion cell had been destroyed. A fringe of thickened glia often followed, and still somewhat farther on the tissue was often in the so-called status spongiosus (fig. 12). This condition

was the same as that seen in the degeneration of tracts in pernicious anemia. The letters *a*, *b*, *c* and *d* in figure 11 indicate the different stages of the process. Near areas of aseptic necrosis or porencephaly one saw also large fat-containing glial cells lying in little heaps of a more or less alveolar shape (figs. 13). Figure 14 shows a cavity on both sides in the lateral nucleus of the optic thalamus.

In the parts of the brain which had been partially destroyed, a great number of blood vessels were seen. In different places there were fissures, which now and then communicated with the cavities.

Besides these real cavities there were numerous spurious cavities. In van Gieson preparations they showed clearly. The sulci between the microgyric convolutions were deep; culdesacs with a narrow entrance were formed (figs. 10 and 15). In these spaces there was often a rete of small blood vessels with proc-

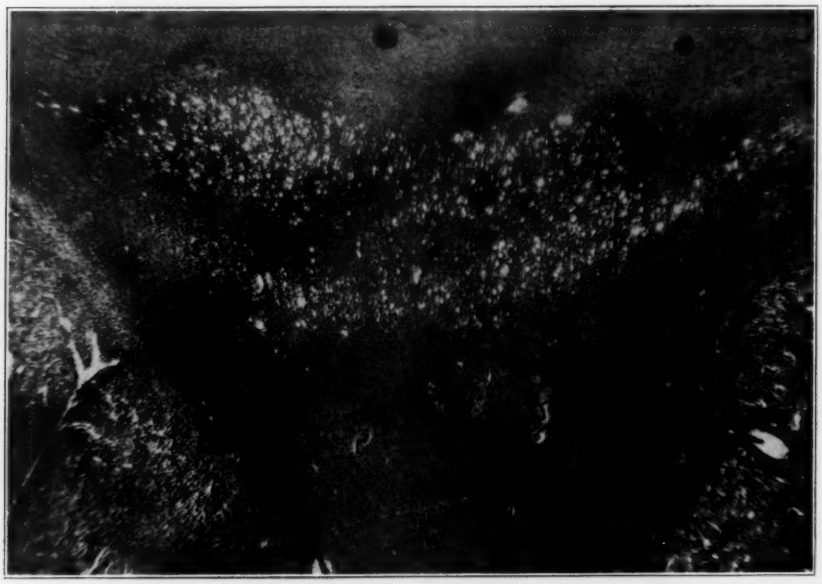

Fig. 12 (case 1).—Status spongiosus in the lateral wall of the cornu posterius; van Gieson stain.

esses in the adventitial layer and new growth of the elements of the connective tissue in the pia and arachnoidea. Now and then the visceral layer of the arachnoidea was seen to be thickened. In this rete granulocytes were present, their number increasing in proportion as the underlying parts of the brain were destroyed by the porencephalic process. In these spurious cavities there were also mononuclear cells resembling lymphocytes, and in some spots erythrocytes were also seen, either close together or solitary. These red blood corpuscles looked fresh; they had not changed. In my opinion, they lay outside the vessels, because when the brain was removed from the skull some vessels were ruptured. This factor is of great value in giving an opinion about the histologic preparations, as was also pointed out by Waitz.[5]

5. Waitz, Robert: Les lésions cérébroméningées à la naissance, Paris, Gaston Doin & Cie, 1931.

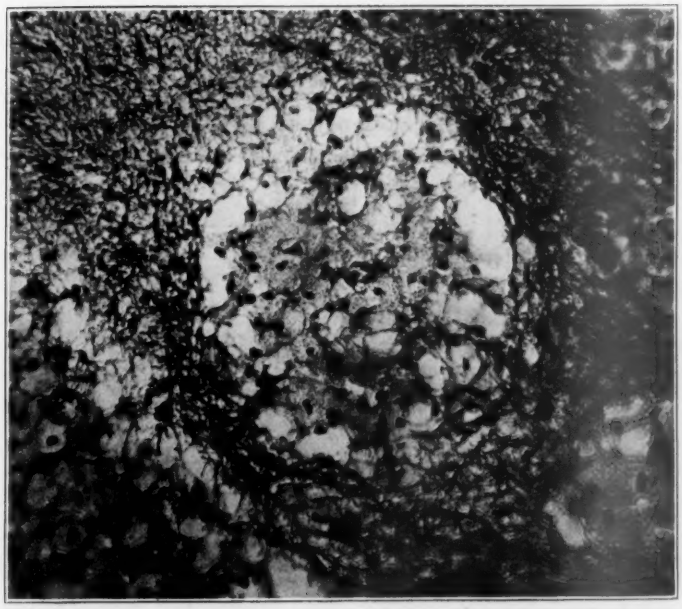

Fig. 13 (case 1).—Beginning of destruction in the cortex, showing a mass of fat-containing glial cells in the medulla corticis of the occipital lobe; hematoxylin-eosin stain.

Fig. 14 (case 1).—Cavities on both sides of the optic thalamus; van Gieson stain.

Extensive studies of the pathologic histology of the porencephaly caused by injuries at birth have been made by Spatz,[6] Siegmund,[7] Schwartz [8] and others.

To be justified in making the diagnosis of hemorrhage due to injury at birth, the examiner must have observed remnants of these hemorrhages in the brain, provided death occurred within the first year of life. Landé [9] rightly claimed that during the first days or weeks of life fresh extravasations or extravasations in the process of being resorbed are present in the meninges, ventricles or substance of the brain. Later there must be remnants in the form of brown spots or deposits of pigment, which may be observed up to the end of the first year and even afterward in the adventitial layer of the blood vessels. Also, localization of the process in the places of predilection reported by Schwartz (in

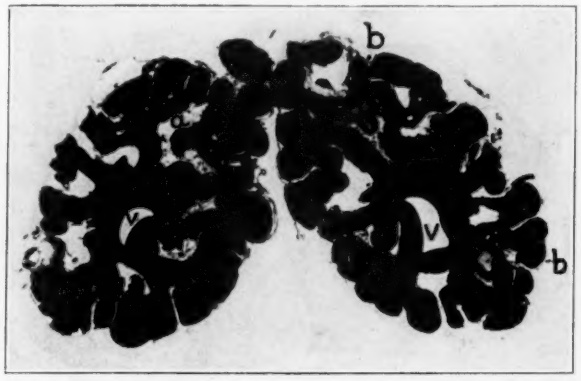


Fig. 15 (case 1).—Occipital pole of the brain, showing: *a*, real cavities; *b*, spurious cavities, and *v*, ventricle; van Gieson stain.

the central convolutions and near the ventricles) may support the probability of a hemorrhage.

I did not find any remnant of a hemorrhage in patient 1. However, injury at birth does not necessarily lead to a hemorrhage; it is possible that contusions, as, for instance, those due to a series of small concussions of the brain, may cause porencephaly or aseptic necrosis. Perhaps one can make a diagnosis of the latter condition immediately after birth from the presence of *Körnchenzellen,* but later it is impossible. There are several factors, then, which may lead to degeneration of the brain. Moreover, the intra-uterine origin of porencephaly certainly comes in for consideration.

6. Spatz, H.: Ztschr. f. d. ges. Neurol. u. Psychiat. **53**:363, 1920.
7. Siegmund, H.: Virchows Arch. f. path. Anat. **241**:237, 1923.
8. Schwartz, P.: Ztschr. f. d. ges. Neurol. u. Psychiat. **90**:263, 1924.
9. Landé, L.: Ztschr. f. Kinderh. **44**:535, 1927.

The extensive studies of the authors cited and the description of my own preparations, as given in this article, relieve me of the duty of going into more detail. I only want to lay stress on the fact that in my case real microgyria existed.

Examination of the frontal serial sections of the brain, stained by the Weigert-Pal and van Gieson methods, led to the following conclusions:

The centrum semiovale Vieussenii was undersized and contained only sparse fibers, which had mostly degenerated and which often showed large swellings of the myelin sheaths. Often they were still larger than those seen in figure 16 indicated by the letter *a*. The stratum sagittale externum et internum of the

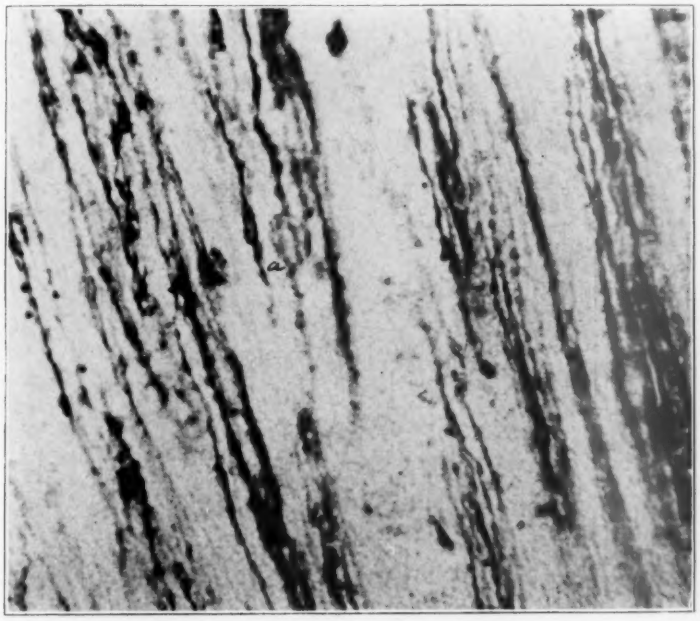


Fig. 16 (case 1).—Degeneration of nerve fibers in the centrum semiovale Vieussenii, showing varicose swelling of the myelin sheath (*a*); Weigert-Pal stain.

frontal brain was without degeneration in its ventral part and radiated into the basal convolutions in the normal way. The sparse fibers of the dorsal part, however, had degenerated. Some fibers which were situated on the interior side of the ventricle at this level and which perhaps represented a poorly developed rostrum corporis callosi had also degenerated. One could not say with certainty (and the same holds true for the other parts of this brain) how many of the nerve fibers had not been formed and how many had degenerated.

In the frontal part of the brain the porencephalic processes were seen in numerous parts of the cortex and medulla corticis.

The corpus callosum was thin over its whole course. In comparison with their surroundings, the myelin sheaths of the gyrus callosus marginalis made a favorable impression, though a small number of them had also degenerated. The cingulum

was hardly visible. The pedunculus septi pellucidi was well developed, though its dorsal part contained some degenerated fibers. In the sections stained by the Weigert-Pal method the capsula interna was hardly visible in its frontal part; the capsula externa and extrema were somewhat better developed. The claustrum, which had broadened in its ventral part, showed a cavity (figs. 17 and 18). In the same figures one sees the contrast of the thin corpus callosum with the broad fornices. The fornices run a separate course.

In the region where normally the nucleus caudatus is situated under the ependyma of the ventricle, a large mass of darkly stained small round cells was found; then came a fringe of hypertrophied glia, but ganglion cells were lacking,

Fig. 17 (case 1).—Section showing the underdeveloped striatum, the thin corpus callosum and the hypertrophied fornix; Weigert-Pal stain.

and the whole part representing the nucleus caudatus was extremely small (fig. 17). I am inclined to regard this mass of small cells as a germination center containing undifferentiated forms. It would then be of the same nature as the much smaller infiltrations of cells, so-called Fischl infiltrate, which I observed diffusely spread through this brain. Perhaps they manifest a developmental inhibition, or perhaps they are normal at this age.[10] In the inferior corner of the lateral ventricles were small holes lined with ependyma, which I believe to be remnants of an ependymitis. The putamen was small, and revealed cavities; ganglion cells were almost totally lacking, and the sparse nerve fibers had degenerated. The globus pallidus also

10. Compare Schwarz, H.; Goolker, P., and Globus, J. N.: The Normal Histology of Infants' Brains, Am. J. Dis. Child. **43**:889 (April) 1932.

was small, but two lamellae could be seen, and there were many more fibers than in the putamen. It must be borne in mind, however, that normally the globus pallidus has an abundance of fibers, so there is always a difference between the two. On microscopic investigation, however, most of the fibers of the globus pallidus, especially the fibrae perforantes, proved to be more or less degenerated. There was hardly any retrolenticular capsule (fig. 19).

In its more caudal parts the capsula interna possessed a larger number of fibers, and they had degenerated less than in the frontal parts.

In the optic thalamus the lateral nuclei were most involved in the destructive process. The nuclei anteriores had a swollen appearance and protruded into the third ventricle, which was also somewhat distended, as was the infundibulum. The

Fig. 18 (case 1).—Section from the same level as figure 17, showing the cavity in the claustrum *a*; van Gieson stain.

tela choroidea of the third ventricle was kept intact in the sections. The fornices, which ran a separate course in the more frontal parts of the brain, did not cohere, but they were united by a small filament. A small cavity existed, the corpus callosum forming the roof.

At the level where the fornices bent down in the direction of the fimbriae they lost their broadness. The splenium corporis callosi was still visible, though much reduced. Of the forcipes and the tapetum hardly anything could be seen.

The optic radiation and the stratum sagittale externum were well developed in their frontal parts; in the occipital part of the brain, however, they showed symptoms of degeneration.

To the naked eye the temporal lobes appeared well preserved in the sections. Their three convolutions could be discerned. The cornu inferius of the lateral

ventricle presented itself soon on microscopic investigation. However, there were cavities, status globosus and degenerated nerve fibers in the temporal lobes, and, because of this, many glial cells laden with fat (*Transportzellen*) had found their way to the pia. Yet the temporal lobes belonged to the better preserved parts of this brain.

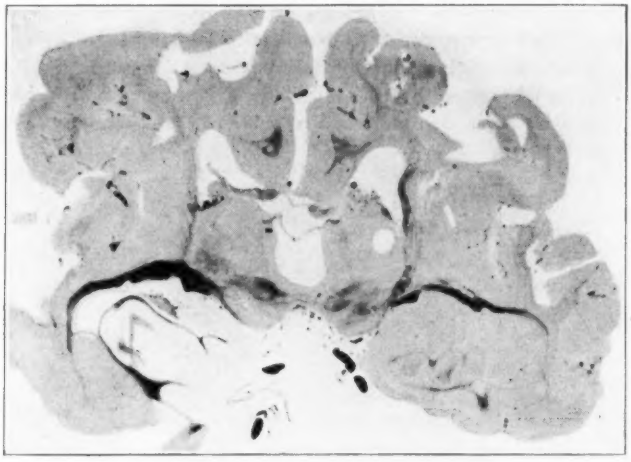

Fig. 19 (case 1).—Beginning of red nuclei; Weigert-Pal stain.

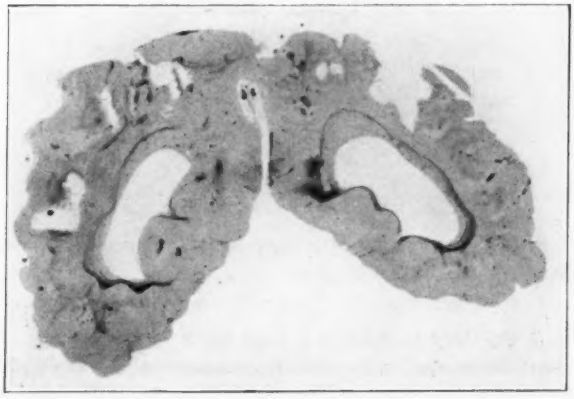

Fig. 20 (case 1).—Occipital lobes; Weigert-Pal stain.

The corpora subthalamica were small on both sides and looked pale in the sections stained by the Weigert-Pal method. A number of fibers could be seen microscopically, but almost all of them had degenerated. The pedes pedunculi were small, but their fibers were in good condition. The impression was that the degenerated fibers had stopped short in their downward course and had not partaken in the formation of the pedes pedunculi. The substantia nigra and the corpora geniculata seemed normal.

The occipital lobes belonged to the most ravaged parts of this brain. The porencephalic process could be studied here in all its particulars (figs. 15 and 20). In several spots the fibrous neuroglia had increased.

There was a marked difference between these degenerated or badly developed parts of the brain and those of the basis cerebri. The nucleus basalis and the substantia innominata might even be called hypertrophic. The different commissurae, the taenia thalami, the ganglion habenulae, the tracts of Vicq d'Azyr and of Meynert, the optic nerves, the chiasma opticum and the optic tracts, the amygdala and cornu ammonis, the red nucleus and the black field of Wernicke were well myelinated and well developed on both sides. The epiphysis also was normal. Figure 21 shows clearly the difference between the dorsal and the ventral parts of the brain.

The Brain Stem and Cerebellum: Examination of the brain stem and the cerebellum led to the following conclusions: The nuclei of the cranial nerves and the cranial nerves themselves were normal. The pyramidal tracts were small and

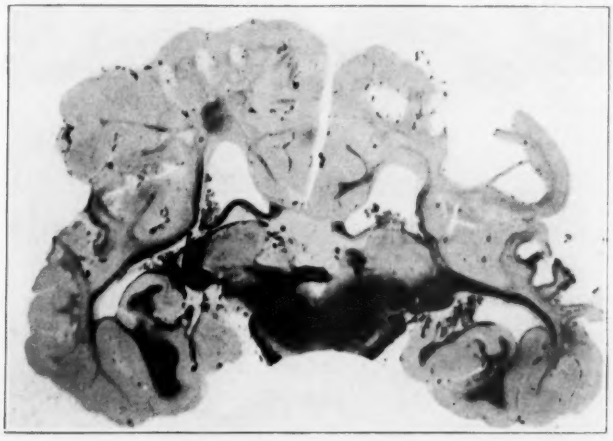

Fig. 21 (case 1).—Normal myelinization of the ventral parts of the brain; Weigert-Pal stain.

appeared pale on staining by the Weigert-Pal method; the same was true of the pyramids themselves. The fasciculus longitudinalis posterior and the corpora quadrigemina were normal. The corpora restiformia, the brachia pontis, the bridge itself and the brachia conjunctiva were small but without signs of degeneration. The lemnisci were also small; the lateral one was better developed than the medial one. The corpus trapezoideum and the superior olive were remarkably well developed. In general, in man the lateral loop of the latter is broader than the medial one, but in this brain the contrary was the case.

The fourth ventricle was slightly distended; there was a slight inflammation of the plexus, and the ependyma, especially in the lateral corners, showed small isolated cavities.

The nuclei tecti and emboliformes were well developed; it was difficult to separate the globosi from their surroundings.

The lobi ansiformes of the cerebellum were undersized, as were the cerebellar olives. In comparison with normal preparations, the ganglion cells were somewhat

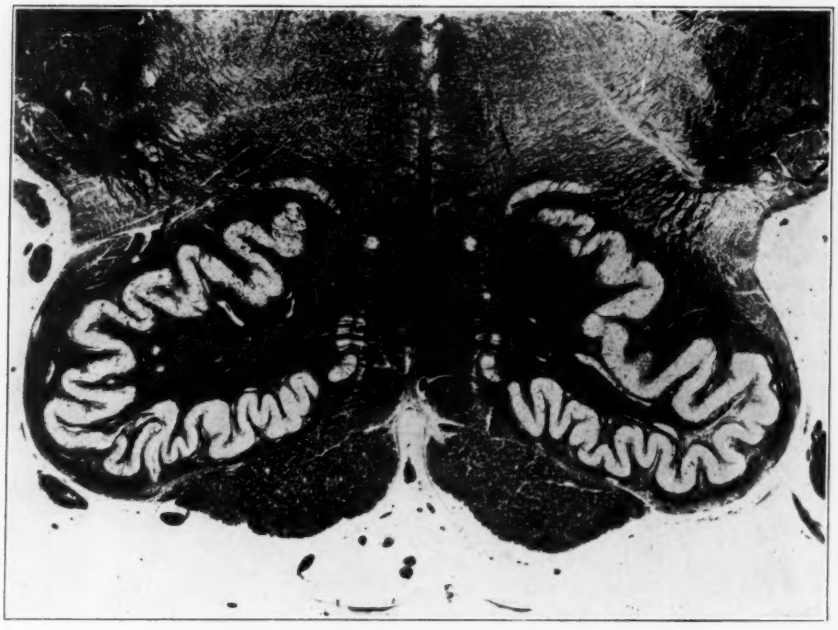

Fig. 22.—Olives and pyramids in a normal child 7 months old; Weigert-Pal stain.

Fig. 23 (case 1).—Section showing underdevelopment of the pyramids and a difference in form between the dorsal and the ventral half of the olives; Weigert-Pal stain; same magnification as figure 22.

diminished in number; the fleece of the cerebellar olive was small and appeared pale on staining by Weigert-Pal's method. The fibers, however, had not degenerated.

Something remarkable was noted in the inferior olives. Sections from the brain of a normal child and from that of patient 1 are shown in figures 22 and 23, respectively, under the same magnification. The difference in age between the two children was three months, but this does not suffice to explain the great difference in size. The striking fact, however, is that in patient 1 in all the sections the dorsal loop showed far fewer windings and much broader ones than the ventral loop, on both sides. Normally there is a difference between the loops, but in this instance it was great. The accessory olives were well developed.

## COMMENT

In the interpretation of this case one is besieged by numerous questions.

The existence of a widely spread porencephalic process and underdevelopment or inhibition of the striatum, especially the neostriatum, may be taken for granted. Moreover, some anomalies were present which can be regarded only as vitia conformationis. It is known that the hypertrophy of the muscles was congenital, that another child of the same parents had a congenital deformity of the brain (probably anencephaly) and that there was a family history of other congenital anomalies of the central nervous system (a child of the mother's brother had spina bifida).

The first questions which arise are: Was the process of porencephaly or aseptic necrosis congenital or was it the sequel of an injury at birth. If the former was the case, did the process progress after birth?

There is no doubt that the majority of porencephalic processes are the sequel of injuries at birth. However, attention has been drawn repeatedly to the fact that other anomalies are observed simultaneously with the porencephaly which doubtless have their origin in an early intra-uterine period, as, for instance, heterotopias. Therefore Schob,[11] partly on the basis of his own investigations, was of the opinion that in a minor number of the cases of porencephaly an intra-uterine origin may be taken for granted. Excluding syphilis, it seems highly improbable that infection, injury, thrombosis and embolus are causative factors. Primary degeneration is most likely, perhaps progressing after birth.

Injuries at birth are met with in normal children born at full term, but they are much more frequent in premature infants. Of the four patients with muscular hypertrophy and extrapyramidal motor disturbances studied, only one was a premature child. It seems most unlikely that all three of the children who were born normally at full term should have suffered from a severe injury at birth. Moreover, motor

11. Schob, F.: J. f. Psychol. u. Neurol. **40**:365, 1930.

disturbances of the pyramidal type were practically lacking, and it is well known that Little's disease is a common occurrence after injury at birth. In patient 1 the central convolutions were not among the most ravaged parts of the brain, and the part of the internal capsule corresponding with them had a better aspect than the capsule or the corona radiata in the more frontal parts of the brain. Furthermore, the symmetry of the necrotic processes is against injury at birth as the causative factor.

That a porencephalic process can begin after birth with acute symptoms seems likely, according to Meyer's [12] observation.

Spatz,[6] in his investigations on the spinal cord of new-born rabbits, came to the conclusion that the specific reaction of the nervous system to trauma is the early appearance of necrosis and cavities, without the formation of scars, and the rapid disappearance of *Körnchenzellen.* These conclusions, though doubtless of great interest, cannot be applied to the new-born infant without great limitations, as has been pointed out by Siegmund [7] and Schob,[11] among others.

In arguing that the process is partially of recent date in patient 1, I may lay stress, first, on the fact that some of the cavities were new, as they were filled with fluid, lacked a membrana limitans gliae accessoria and had walls lined with *Körnchenzellen.* Second, part of the varicose swellings of the myelin sheaths, especially in the centrum semiovale, were large, and, as is well known, these structures are extremely tender and are soon totally destroyed. Also, the reaction of the pial connective tissue and the adventitial layer of the pial blood vessels and the presence of status spongiosus in several places in the brain were indications of a still active process. However, empty cavities could also be seen, bordered by a membrana limitans gliae accessoria, and in the brain the fibrous neuroglia had increased. According to the mother, the child became still more rigid after its dismissal from the clinic. The latter fact also indicates that the process had begun before birth and that it was progressive.

In brains which have undergone injury at birth, the basal parts are generally much better preserved than the dorsal parts.

It is a remarkable fact that this was also the case in the brain of patient 1. If one takes for granted that the beginning of the porencephalic process dated from before birth and that it was progressive after birth, the question arises whether all the anomalies were a result of it. This is true for all the parts of the brain which were primarily or secondarily destroyed. Before birth and also in the first period after birth certain parts of the brain have an influence as formative stimuli on the development of other parts. When these stimuli

12. Meyer: Jahrb. f. Kinderh. **76**:552, 1912.

are absent, developmental inhibitions may be observed. The association of real microgyria and porencephaly, which is repeatedly met with, is explained in this way. One may ask whether in my case (this being the *cardo questionis*) the striatum was underdeveloped because the formative stimuli for its development were lacking, or whether this deformed part of the brain was easily attacked by a process of degeneration. In my opinion, the latter holds true, and again I cite arguments from the clinical data. Three of the four children were born normally at full term. Therefore, it seems highly improbable that all three had undergone a severe injury at birth, attacking in either a primary or secondary way the striatum, and especially the neostriatum, or that an intra-uterine porencephalic process had been present in all three. It seems much more reasonable to assume that in these cases of congenital muscular hypertrophy another deformity was also present, viz., a malformation of the striatum.

Several authors are inclined to regard the diseases of the striatum investigated by C. Vogt and O. Vogt [13] as caused by injuries at birth. Status dysmyelinatus is called by Cécile Vogt "das Ergebnis eines pathologischen Prozesses, welcher unter gleichzeitiger Volumenverminderung zu einer Verarmung der striären Markfaserung führt und zwar besonders im Gebiet des Pallidum" (the result of a pathologic process which, with a simultaneous decrease in volume, leads to atrophy of the striated medullary fibers, especially in the region of the pallidum). My case does not belong to this class. During the life of the children there were no athetosic movements, and after death the most significant processes were not observed in the pallidum.

The poor development of the corpus subthalamicum, which was surrounded by normal parts, also points in my case to a congenital inhibition, perhaps in connection with the pathologic process of the striatum.

In the brain of patient 1 several anomalies were observed which cannot be explained by the lack of formative stimuli, unless one hypothesizes a disharmony by which some parts received extra stimuli or by which inhibiting influences were counteracted. The theory, however, is rather nebulous.

On macroscopic examination of the brain, striking facts were the overdevelopment of the gyrus supramarginalis and the gyrus angularis and the good size of the paleocerebellum, as compared with the small neocerebellum, thin corpus callosum and broad fornices. There proved to be hypertrophy of the nucleus basalis and substantia innominata, the superior olives and the corpus trapezoideum and a peculiarity in the loops of the inferior olives.

13. Vogt, Cécile, and Vogt, Oskar: J. f. Psychol. u. Neurol. (supp. 3), vol. 25, 1920.

All this cannot be explained by a porencephalic process limited to the hemispheres.

Finally, one must ask the cause of the hydrocephalus, which was moderate and which proved to be hydrocephalus communicans. The explanation is generally given that the hydrocephalus in porencephaly is caused by sclerotic processes and abnormal development of the brain. This may also be partly true in my case, but the large number of cells present in the pia-arachnoid may have impeded the resorption of the spinal fluid and hence cannot be disregarded as a causative factor.

Is there any connection between the muscular hypertrophy and the cerebral process? Bruck [2] seemed to favor this theory. Pachantoni [14] reported the case of a man, aged 25, who had suffered an injury of the occiput and who, after the lapse of a year, presented real hypertrophy and feebleness of the contralateral leg (*myohypertrophie essentielle adynamique*). This author also was inclined to look for a connection between these conditions. I cannot explain the connection in my cases, but I am firmly convinced that there must be more than a simple syntropy.

SUMMARY

A clinical entity exists in which congenital muscular hypertrophy, extrapyramidal motor disturbances and mental deficiency are found. Three children whose families were not related came under observation at the Children's Clinic of the University of Amsterdam. The report of a fourth case was found in the literature. In one of these children extensive examination of the brain was possible. The explanation is given that in these cases malformation of the striatum was primary and that the porencephalic process found in the patient must be regarded as accidental, attacking an inferior brain. Further postmortem examinations will show whether this surmise is right.

14. Pachantoni, D.: Schweiz. Arch. f. Neurol. u. Psychiat. **3**:119, 1918.

# A NEW AUXILIARY TREATMENT FOR IMPETIGO CONTAGIOSA

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AND
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The contagious and auto-inoculable character of the pyogenic infections of the skin causes a great deal of inconvenience, especially in school children, among whom dissemination both by direct and by indirect contact occurs readily. The interchange of pencils, pens, playthings, etc., assumes an important rôle in this contagion.

Inconvenience is occasioned by the loss of time incurred when, after a diagnosis of pyogenic infection is made, the pupil is excluded from classroom activities.

The most important of the group of pyogenic infections is impetigo contagiosa, but under this grouping we include ecthyma and infectious eczematoid dermatitis also.

Impetigo contagiosa is caused by invasion of the upper strata of the skin by staphylococci or streptococci. The condition begins in the form of small or large blisters. The roof of such a blister is very thin, so that on the slightest injury it ruptures. The content of the blister, which is a seropurulent material, dries on the raw, denuded base of the blister and is also carried to other portions of the skin, as a result of which new lesions usually arise.

The exposed parts, such as the face, hands, ears, and neck, are the most frequent sites of this infection.

Ordinarily, once the diagnosis is established, difficulty arises in attempting to control the spread of the infection. The chief reason for this lies in the fact that the application of occlusive dressings, especially on the face, neck and ears, requires the use of adhesive tape. It is a common experience to find the impetiginous infection spreading where the tape has been fastened to the skin. To leave the affected surface uncovered except by the medicament applied leads to dissemination, because the crusts are usually carried to immediately adjacent or more distant areas of the skin surface.

It was because of these difficulties that our problem arose, that is, to find an occlusive antiseptic dressing, easily applied and without the

From the Pittsburgh Skin and Cancer Foundation.

disadvantages referred to. Our studies resulted in the selection of metaphen 1 : 500 incorporated in flexible collodion, which was prepared for us by the Dermatological Research Laboratories of Philadelphia.

A brief résumé of the method of application and the results is submitted.

## METHOD OF APPLICATION

The skin surface surrounding the infected area is washed with soap and water and dried thoroughly with absorbent tissue. The lesion is painted with several layers of metaphen 1 : 500 in collodion, which is permitted to dry layer by layer.

In twenty-four hours the easily removable layers of the metaphen-collodion mixture are removed with a tissue forceps. The adherent part is left on, and the mixture is reapplied in several layers. The procedure is repeated on the third day.

*Clinical Trials and Results*

| Drug Used | Disease | Number of Patients Treated | Average Duration Before Treatment, Days | Average Duration of Treatment, Days | Failures, per Cent |
|---|---|---|---|---|---|
| 1. Metaphen 1:500 in collodion | Impetigo contagiosa | 234 | 10 | 8 | 15 |
| | Ecthyma..... | 10 | 28 | 14 | 25 |
| | Infectious eczematoid dermatitis (pustular and impetiginous eczema)..... | 20 | 21 | 20 | 0 |
| | Control Experiments | | | | |
| 2. Flexible collodion, unmedicated | Impetigo contagiosa | 10 | 10 | 14 | 20 |
| 3. Mercurochrome 4 per cent followed by flexible collodion | Impetigo contagiosa | 10 | 10 | 14 | 30 |

On the fourth day all of the metaphen-collodion preparation, which by that time has curled up at the edges, is removed, and with it the underlying encrustation. If the underlying skin is dry, light anointing with 2 per cent ammoniated mercury is carried out. If, however, the surface is still moist, the metaphen-collodion mixture is applied for another period of three days.

## RESULTS

A summary of the results obtained is given in the accompanying table. Two outstanding results were obtained which need special mention:

CASE 1.—L. C., aged 60, presented an infectious eczematoid dermatitis of several months' standing which originated from a furuncle of the arm. The condition affected both upper extremities. Previous to the metaphen-collodion treatment, antiseptics in the form of wet dressings, lotions and ointments and irradiation both with roentgen and with ultraviolet rays, were used, but the condition became worse. Three days after the metaphen-collodion paintings, both the infection and the dermatitis subsided, and in seven days the patient was entirely relieved.

CASE 2.—Miss V. M., aged 21, presented an acute impetiginous dermatitis affecting the face and neck, causing a great deal of discomfort, with a feeling of tightness and intense itching. The condition was unsightly. After seven daily metaphen-collodion paintings the patient was able to resume her occupation as a secretary.

## ADVANTAGES OF THE TREATMENT

The advantages of the use of the metaphen-collodion preparation are:

1. The ease of application.

2. The impervious character of the dressings, easily confining the infection, so that auto-inoculability and contagion become less likely and thus the disease does not necessitate the exclusion of school children from their classroom activities, except in unusually severe cases.

## SUMMARY

The use of metaphen 1 : 500 in collodion has been introduced for the treatment of pyogenic infections of the skin. The results obtained were so satisfactory that this treatment is presented as an auxiliary one for impetigo contagiosa, ecthyma, and infectious eczematoid dermatitis (pustular eczema and impetiginous eczema).

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# ACETARSONE IN THE TREATMENT OF CONGENITAL SYPHILIS

## A COMPARISON WITH BISMUTH THERAPY

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Certain disadvantages must have been noted by those who have had experience with the usual methods employed in the treatment of congenital syphilis. Among these may be mentioned: (*a*) the reluctance with which parents submit their children to treatment, with subsequent irregular attendance, and (*b*) the lack of muscular tissue in puny infants, which makes intramuscular injection difficult or impossible. Therefore, acetarsone, being a drug that can be given perorally, promised to lead to a decided step forward. To determine its efficacy I have used it exclusively in a group of infants and children for the past two years.

Acetarsone [1] is not a new drug. It has been used in amebic dysentery,[2] pemphigus,[3] yaws,[4] Vincent's angina,[5] parasitic infestations,[6] malaria [7] and other conditions; but as this paper primarily deals with its use in congenital syphilis, I shall briefly review its history from that standpoint.

Few references to acetarsone can be found in the literature from the time of its discovery until 1921. At this time Fourneau [8] revived interest in the drug by publishing his experiences with its use in spirochetal and trypanosomal infections.

The first report of its effect on congenital syphilis was made by Guillemot [9] in 1924. He described its use in the treatment of an 11 month old infant with condylomatous lesions and fissure of the upper lip. He noted a rapid disappearance of the lesions. In the same year

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From the Department of Pediatrics of the Jefferson Medical College.

1. Merck and Company furnished the acetarsone used in this study.
2. Johs, F. M., and Jamison, S. Chaille: New Orleans M. & S. J. **77**:469 (May) 1925.
3. Kromayer: Sechs durch Spirocid geheilte Pemphigus Fälle, Deutsche med. Wchnschr. **55**:229 (Feb. 8) 1929.
4. Tanon and Jamot: Le traitement du pian par le stovarsol, Rev. de méd. et d'hyg. trop. **21**:18 (Jan.) 1924.
5. Moncany: Rev. gén. de clin. et de thérap. (j. d. prat.) **40**:64 (Jan. 23) 1926.
6. Perrin, M.: Rev. méd. de l'est **54**:94 (Nov. 15) 1926.
7. Valenti, F., and Tomaselli, F.: Policlinico **32**:1629 (Nov. 23) 1925.
8. Fourneau, E.: Ann. Inst. Pasteur **35**:571, 1921.
9. Guillemot, L.: Bull. Soc. de pédiat. de Paris **22**:211, 1924.

Dupérié, Cadenaule and Clarac [10] used it successfully in treating a 2 month old infant who exhibited marked signs of syphilis.

In 1925, Krösl [11] stated that of three infants treated, in only one was the Wassermann reaction reversed, while in two it remained positive.

Marfan [12] in his report advised a dose of 0.02 Gm. per kilogram of body weight and recommended that it be given on four consecutive days of each week for from six to eight weeks. He noted the occurrence of diarrhea and erythema of the buttocks in several cases.

Soldin and Lesser [13] in their cases began with a dose of 0.25 Gm. twice daily and then gave it four times daily to children up to 2 years of age. They noted a rapid recession of the maculopapular exanthem, just as follows the use of arsphenamine. Twenty-four hours after the administration of two doses, no living spirochetes were found in the serum or lesions, and within forty-eight hours no spirochete bodies were observed. Two cases ended fatally, but this was attributed to intercurrent infections rather than to the use of acetarsone.

Juarros and Galaraetta,[14] in 1927, and Ginella [15] and Oppenheim and Fessler,[16] in 1928, reported favorable experiences.

Tuscherer,[17] in 1929, stated that the majority of the references in the German literature to the use of acetarsone in the treatment of congenital syphilis were favorable. From his own experience, he concluded that the treatment was the equal of injections of arsphenamine and mercury. He adopted the following schedule:

| No. Days | No. Doses | Dose, 0.25 Gm. Tablets |
|---|---|---|
| 3 | 1 | ¼ |
| 3 | 2 | ¼ |
| 3 | 3 | ¼ |
| 3 | 4 | ¼ |
| 3 | 3 | ½ |
| 3 | 4 | 1 |
| 3 | 2 | 1 |
| 20 | 3 | |

Following this plan of treatment, the cutaneous manifestations cleared up within from ten to twelve days.

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10. Dupérié; Cadenaule and Clarac: Gaz. hebd. d. sc. méd. de Bordeaux **45:** 456 (July 20) 1924.

11. Krösl, H.: Versuche und Erfahrungen mit Stovarsol und Spirocid, Wien. klin. Wchnschr. **37:**1209 (Nov. 20) 1924.

12. Marfan, P.: Rev. gén. de clin. et de thérap. **2:**289, 1925.

13. Soldin, Max, and Lesser, Fritz: Deutsche med. Wchnschr. **51:**991 (June 12) 1925.

14. Juarros, C., and Galaraetta, P.: Siglo méd. **80:**653 (Dec. 31) 1927.

15. Ginella, A.: Biol. med. **18:**78 (March) 1928.

16. Oppenheim, M., and Fessler, A.: Arch. f. Dermat. u. Syph. **159:**549, 1928.

17. Tuscherer, J.: Monatschr. f. Kinderh. **45:**62 (Sept.) 1929.

In 1930, Bratusch-Marrain [18] compared the results in fifty-one children with syphilis treated with neoarsphenamine and mercury with those in forty-seven patients treated orally with acetarsone. Of the former group 29.4 per cent gave a negative Wassermann reaction following treatment while in 42.2 per cent of the latter group the reaction became negative.

He pursued the following schedule:

| No. Days | Dose, Gm. per Kg. |
|---|---|
| 7 | 0.005 |
| 7 | 0.010 |
| 7 | 0.015 |
| 42 | 0.020 |

Three such courses were given, with a four to six weeks rest period between courses. He reported the occurrence of a Jarisch-Herxheimer reaction in one case but concluded that the administration of acetarsone was the treatment of choice for syphilis in childhood.

Kiss [19] employed a single course of acetarsone during the first year of life, or until the infants could be expected to tolerate injections of neoarsphenamine and bismuth preparations. Of eighteen cases studied, in 39 per cent the Wassermann reaction became negative. Vomiting occurred in two instances, and diarrhea in four, but these complications were not severe. Regardless of the patient's age he administered the drug as follows:

| No. Days | No. Doses | Dose, 0.25 Gm. Tablets |
|---|---|---|
| 7 | 1 | ¼ |
| 7 | 2 | ¼ |
| 7 | 3 | ¼ |

The third dosage was continued for three months. A two month rest period was allowed, and then injections of neoarsphenamine and a bismuth preparation were begun regardless of any change in serologic reaction.

Among the more recent reports may be mentioned those of Klaften,[20] Nedelman [21] and Blechman.[22]

Up to this time, it will be observed that these reports have emanated from foreign investigators. Despite the extensive use of the drug in Europe, it has been little employed in America.

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18. Bratusch-Marrain, Alois: Arch. f. Kinderh. **92**:26 (Nov. 28) 1930.
19. Kiss, Paul V.: Jahrb. f. Kinderh. **126**:211, 1930.
20. Klaften, E.: Med. Klin. **27**:1208, 1931.
21. Nedelman, E.: Jahrb. f. Kinderh. **134**:89 (Dec.) 1931.
22. Blechman, G.: Hôpital **20**:3 (Jan.) 1932.

The first paper to be published in this country was that of Cregor and Gastineaux,[23] who successfully used acetarsone in the treatment of fifteen adults with syphilis. The first American report of its effect on congenital syphilis was made by Mettel,[24] in 1931, who used it in cases of syphilitic periostitis in children. He noted a clinical improvement but no change in the Wassermann reaction. Abt and Traisman, in a preliminary report [25] in February 1932 and in a subsequent one [26] in August of the same year, concluded that acetarsone in congenital cases is an effective and rapid antisyphilitic agent. They recorded one case of exfoliative dermatitis as a result of therapy.

About this time Maxwell and Glaser,[27] while reporting favorable results, prescribed caution in the use of the drug. They described toxic neurologic symptoms as a result of acetarsone therapy, with one recovery and one death. In addition they cited Martin's two cases of flaccid paralysis following such treatment.

Simultaneously with the preceding report, Rosenbaum [28] noted satisfactory results in forty-one cases.

To these reports I desire to add the experience that I have had with acetarsone during the past two years.

Only those patients who were undoubtedly syphilitic and who had received no antisyphilitic treatment were selected for this study. Blood tests were made at the beginning and at the termination of each nine week course of treatment.

## DOSAGE AND ADMINISTRATION

Acetarsone is a pentavalent arsenic compound. It is closely related to arsphenamine in its chemical composition. Its arsenic content is from 27.1 per cent to 27.4 per cent, as compared to about 20 per cent for neoarsphenamine and 21 per cent for sulpharsphenamine. It is a white crystalline powder, easily soluble in water, tasteless and easily digested. It is marketed in 0.1 and in 0.25 Gm. tablets.

The dosage used was patterned after that of Bratusch-Marrain. For the first week, 0.005 Gm. daily for each kilogram of body weight was given; for the second week, 0.01 Gm.; for the third week, 0.015 Gm., and for the following six weeks, 0.02 Gm. It is dissolved in water or preferably in milk and given one-half hour before feeding. If the quantity is small, it is given only once daily, but as the infant requires a larger dose it is divided into two or three doses daily.

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23. Cregor, Frank W., and Gastineaux, Frank M.: Stovarsol in the Treatment of Syphilis: Preliminary Report, Arch. Dermat. & Syph. **15**:43 (Jan.) 1927.

24. Mettel, Howard B.: Arch. Pediat. **48**:761, 1931.

25. Deleted.

26. Abt, Arthur F., and Traisman, Alfred S.: J. Pediat. **1**:172 (Aug.) 1932.

27. Maxwell, C. H., Jr., and Glaser, Jerome: Treatment of Congenital Syphilis with Acetarsone (Stovarsol) Given by Mouth, Am. J. Dis. Child. **43**:1461 (June) 1932.

28. Rosenbaum, Harold A.: Stovarsol in the Treatment of Syphilis in Infants and in Children, Am. J. Dis. Child. **44**:25 (July) 1932.

### UNTOWARD REACTIONS

As I have previously mentioned, various authors have noted toxic manifestations, such as exfoliative dermatitis, a Jarisch-Herxheimer reaction, vomiting, diarrhea, paralysis and even death. In the present study no severe toxic phenomena were observed. There occurred one case of vomiting, which was promptly controlled by suspension of treatment, and two cases of erythema of the buttocks, which caused no interruption in therapy.

### RESULTS

In the present series, twenty infants and children were treated. One of the striking features in this study was the regularity of attendance.

The patients were divided into two groups, those under 1 year of age (table 1) and those over 1 year of age (table 2). In the first group, the age range was from 2 to 4 weeks with the exception of one infant who was 10 months old. Of these, six were of the asymptomatic group and were suspected of having had the disease because of positive Wassermann reactions in the mothers. Of the remaining four patients, one had a condylomatous lesion on the vulva, one had Parrot's pseudoparalysis of the right arm and two had snuffles. In all cases the Wassermann and Kahn reactions were positive. Two patients received one course of treatment; four, two courses, and four, three courses. Within five weeks all of the lesions were healed or markedly improved. At the end of the first course both the Wassermann and the Kahn reaction became negative in nine instances, while in one the Wassermann reaction was reduced to plus 2 but the Kahn reaction was plus 4. On the completion of the second course, all the patients gave negative serologic reactions. The general physical condition was markedly improved.

In the second group, the age range was from 4 to 12 years. Five of these children presented no symptoms. Of the other five, one showed interstitial keratitis; one, Hutchinson's teeth, and one, a gumma in the left parotid region, and two were subject to epileptiform attacks. The Wassermann and Kahn reactions of nine patients were positive, while one showed a negative Wassermann reaction but a plus 4 Kahn reaction. Four patients received one course of treatment; five, two courses, and one, three courses.

The epileptiform seizures of one patient were completely controlled at the end of the first course, while in the other no improvement was noted. The gumma presented by one patient was completely healed within five weeks. The patient with interstitial keratitis showed some improvement at the termination of the first course. The Wassermann and Kahn reactions became negative in two instances and remained unchanged in eight.

TABLE 1.—*Effect of Acetarsone Therapy on Congenital Syphilitic Patients Under 1 Year of Age*

| Case No. | Age | Symptoms | Reactions | | Course of Treatment | Results | Reactions | |
|---|---|---|---|---|---|---|---|---|
| | | | Wassermann | Kahn | | | Wassermann | Kahn |
| I | 2 wks. | Coryza; mother gave positive reaction | Plus 4 | Plus 4 | 1 | No coryza at end of 4 wks. | Neg. | Neg. |
| | | | | | 2 | No symptoms | Neg. | Neg. |
| | | | | | 3 | No symptoms | Neg. | Neg. |
| II | 2 wks. | Mother gave positive reaction | Plus 4 | Plus 4 | 1 | No symptoms | Neg. | Neg. |
| | | | | | 2 | No symptoms | Neg. | Neg. |
| III | 2 wks. | Mother gave positive reaction | Plus 3 | Plus 1 | 1 | No symptoms | Neg. | Neg. |
| | | | | | 2 | No symptoms | Neg. | Neg. |
| IV | 3 wks. | Mother gave positive reaction | Plus 4 | Plus 4 | 1 | No symptoms | Neg. | Neg. |
| | | | | | 2 | No symptoms | Neg. | Neg. |
| V | 3 wks. | Mother gave positive reaction | Plus 4 | Plus 4 | 1 | No symptoms | Neg. | Neg. |
| VI | 4 wks. | Condyloma of vulva; mother gave positive reaction | Plus 4 | Plus 4 | 1 | Condyloma nearly healed within 5 wks. | Neg. | Neg. |
| VII | 4 wks. | Coryza; mother gave positive reaction | Plus 4 | Plus 4 | 1 | No coryza at end of 5 wks. | Neg. | Neg. |
| | | | | | 2 | No symptoms | Neg. | Neg. |
| | | | | | 3 | No symptoms | Neg. | Neg. |
| VIII | 4 wks. | Mother gave positive reaction | Plus 4 | Plus 4 | 1 | No symptoms | Neg. | Neg. |
| | | | | | 2 | No symptoms | Neg. | Neg. |
| | | | | | 3 | No symptoms | Neg. | Neg. |
| IX | 4 wks. | Parrot's pseudoparalysis; mother gave positive reaction | Plus 4 | Plus 4 | 1 | No evidence of epiphysitis within 4 wks. | Neg. | Neg. |
| | | | | | 2 | No symptoms | Neg. | Neg. |
| | | | | | 3 | No symptoms | Neg. | Neg. |
| X | 10 mos. | Mother gave positive reaction | Plus 4 | Plus 4 | 1 | No symptoms | Plus 2 | Plus 4 |
| | | | | | 2 | No symptoms | Neg. | Neg. |

TABLE 2.—*Effect of Acetarsone Therapy on Congenital Syphilitic Patients Over 1 Year of Age*

| Case No. | Age | Symptoms | Reactions | | Course of Treatment | Results | Reactions | |
|---|---|---|---|---|---|---|---|---|
| | | | Wassermann | Kahn | | | Wassermann | Kahn |
| I | 4 yrs. | Mother gave positive reaction | Plus 4 | Plus 4 | 1 | No symptoms | Plus 4 | Plus 4 |
| | | | | | 2 | No symptoms | Plus 4 | Plus 4 |
| II | 5 yrs. | Mother gave positive reaction | Plus 4 | Plus 4 | 1 | No symptoms | Plus 4 | Plus 4 |
| III | 6 yrs. | Mother gave positive reaction | Plus 4 | Plus 4 | 1 | No symptoms | Plus 4 | Plus 4 |
| | | | | | 2 | No symptoms | Plus 4 | Plus 4 |
| IV | 7 yrs. | Gumma in parotid region | Neg. | Plus 4 | 1 | Gumma healed within 5 wks. | Neg. | Neg. |
| | | Mother gave positive reaction | | | 2 | No symptoms | Neg. | Neg. |
| V | 8 yrs. | Epileptiform attacks; mother gave positive reaction | Plus 4 | Plus 4 | 1 | No symptoms | Neg. | Neg. |
| VI | 11 yrs. | Epileptiform attacks; mother gave positive reaction | Plus 4 | Plus 4 | 1 | No improvement | Plus 4 | Plus 4 |
| VII | 9 yrs. | Hutchinson's teeth; poor mentality; mother gave positive reaction | Plus 4 | Plus 4 | 1 | No improvement | Plus 4 | Plus 4 |
| | | | | | 2 | No improvement | Plus 4 | Plus 4 |
| | | | | | 3 | No improvement | Plus 4 | Plus 4 |
| VIII | 12 yrs. | Interstitial keratitis | Plus 4 | Plus 4 | 1 | Improved | Plus 4 | Plus 4 |
| IX | 11 yrs. | Mother gave positive reaction | Plus 4 | Plus 4 | 1 | No symptoms | Plus 4 | Plus 4 |
| | | | | | 2 | No symptoms | Plus 4 | Plus 4 |
| X | 9 yrs. | Mother gave positive reaction | Plus 4 | Plus 4 | 1 | No symptoms | Plus 4 | Plus 4 |
| | | | | | 2 | No symptoms | Plus 4 | Plus 4 |

### COMPARISON WITH BISMUTH THERAPY

No absolute comparison of the effects of two drugs can be made because of the impossibility of studying their action under precisely the same conditions. For example, one must take into consideration (*a*) the

TABLE 3.—*Effect of Bismuth Therapy on Congenital Syphilitic Patients Under 1 Year of Age*

| Case No. | Age | Symptoms | Wassermann Reaction | Course of Treatment* | Results | Wassermann Reaction |
|---|---|---|---|---|---|---|
| I | 2 mos. | Coryza; pseudo paralysis; dactylitis; on roentgen examination considerable destruction of lower end of radius and ulna | Plus 4 | (1) 10 injections (15 mg.) | After third injection patient began to move wrists and dactylitis began to subside; healed after tenth injection | — |
| | | | | (2) 20 injections (65 mg.); interrupted | No symptoms | — |
| | | | | (3) 20 injections (65 mg.); interrupted | No symptoms for two years | — |
| II | 4 mos. | Coryza; secondary rash—mucous patches | Plus 4 | (1) 20 injections (32 mg.) | After seventh injection lesions completely healed | Plus 2 |
| | | | | (2) 20 injections (65 mg.) | No symptoms | — |
| | | | | (3) 20 injections (65 mg.) | No symptoms for eighteen months | — |
| III | 2 mos. | Emaciation; coryza; mucous patches; desquamation of hands and feet | Plus 4 | (1) 20 injections (65 mg.) | After fourth injection lesions entirely healed; weight stationary for four weeks; then gained 8 ounces weekly | — Child left town |
| IV | 1 yr. | No symptoms; both parents gave positive reactions | Plus 4 | (1) 20 injections (65 mg.); interruption for eight weeks | No symptoms | Plus 1 |
| | | | | (2) 20 injections (65 mg.); interrupted by pertussis | No symptoms | — |
| V | 2 mos. | Secondary rash; enlarged spleen | Plus 4 | (1) 10 injections (65 mg.) | Lesions healed after fourth injection; spleen not palpable | Not taken; left town after 10th injection |

* The doses given in parentheses indicate the amount of metallic bismuth. A preparation of bismuth salicylate in oil was used.

duration of treatment, (*b*) the degree and virulence of the infection and (*c*) the number of cases observed. Bearing these factors in mind, I shall compare the results of acetarsone therapy with those obtained with injections of a bismuth preparation as previously reported.[29]

A study of table 1 and table 3 will reveal a striking similarity in the action of the two drugs. It will be noted that in early infancy all

29. Coppolino, John F.: Bismuth Therapy Exclusively in Congenital Syphilis, Am. J. Dis. Child. **39**:288 (Feb.) 1930.

lesions were rapidly healed and the Wassermann reactions became negative, while at the end of the first year of life the reactions were merely reduced. In 50 per cent of the patients treated with bismuth, the reaction became negative on the completion of the first course, and

TABLE 4.—*Effect of Bismuth Therapy on Congenital Syphilitic Patients Over 1 Year of Age*

| Case No. | Age | Symptoms | Wassermann Reaction | Course of Treatment* | Results | Wassermann Reaction |
|---|---|---|---|---|---|---|
| VI | 10 yrs. | High grade keratitis of right eye; no lesion of left eye | Plus 4 | (1) 20 injections (65 mg.) | Keratitis completely healed by tenth injection; left eye became involved at the third injection but to a lesser degree | — Left town |
| VII | 9 yrs. | Periostitis involving tibias and right femur | Plus 4 | (1) 20 injections (65 mg.) | Periostitis; completely healed by 12th injection | Plus 3 |
| | | | | (2) 20 injections (65 mg.) | No symptoms | Plus 3 |
| | | | | (3) 20 injections (130 mg.) | No symptoms | 4 wks. later plus 2 |
| VIII | 7 yrs. | Poor mentality | Plus 4 | (1) 20 injections (130 mg.) | Some improvement in mentality | Plus 4 |
| | | | | (2) 20 injections (130 mg.) | Mentally same | Plus 4 |
| | | | | (3) 20 injections (130 mg.) | Same | Plus 4 |
| IX | 7 yrs. | Punched-out kidney-shaped ulcer 2½ by 1¼ inches | Plus 4 | (1) 20 injections (130 mg.) | Ulcer completely healed at the 4th injection | Plus 4 |
| | | | | (2) 20 injections (130 mg.) | No symptoms | Plus 4 |
| | | | | (3) 20 injections (130 mg.) | No symptoms | Plus 2 Left town |
| X | 6 yrs. | No symptoms; mother's Wassermann reaction plus 4 | Plus 4 | (1) 20 injections (130 mg.) | No symptoms | Plus 2 |
| | | | | (2) 20 injections (130 mg.) | No symptoms | — Left town |
| XI | 9 yrs. | Marked keratitis of both eyes | Plus 4 | (1) 20 injections (130 mg.) | Improved | Plus 1 |
| | | | | (2) 20 injections | Improved | Plus 3 |
| XII | 8 yrs. | No symptoms; both parents syphilitic | Plus 1 | (1) 20 injections (130 mg.) | No symptoms | — |
| | | | | (2) 20 injections | No symptoms | — |
| XIII | 9 yrs. | No symptoms; mother's Wassermann reaction plus 4 | Plus 1 | (1) 20 injections (130 mg.) | No symptoms | — |
| | | | | (2) 20 injections (130 mg.) | No symptoms | — |

* The doses given in parentheses indicate the amount of metallic bismuth.

in 100 per cent, at the end of the second course. Of those treated with acetarsone, 90 per cent gave negative reactions at the termination of the first course, and 100 per cent, at the end of the second course.

In the older group, all of the lesions were improved within the same period of time. The Wassermann reaction was reversed in three (37.5 per cent) of those treated with bismuth, two of whom had a

plus 1 reaction at the beginning of treatment. It became negative in two (20 per cent) of the children treated with acetarsone, and was unchanged in the others.

## CONCLUSIONS

1. Acetarsone, in the dosage recommended, is well tolerated by infants and children.

2. It is administered with ease. There was no break in the continuity of attendance with this plan of treatment.

3. It is extremely effective for young infants, both rendering them symptom-free and causing the serologic reactions to become negative.

4. It is not so efficacious in the treatment of older persons, being more useful in causing clinical improvement than in reversing the serum reaction.

5. It is equal to bismuth in its ability to heal lesions but appears to be superior in its ability to bring about an earlier reversal of the serum reaction.

6. It appears to be the drug of choice for young syphilitic infants.

# VIOSTEROL IN THE PROPHYLAXIS OF RICKETS IN PREMATURE INFANTS

## CLINICAL, CHEMICAL AND ROENTGENOLOGIC OBSERVATIONS

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In spite of the advances made in the prophylaxis of rickets in the full-term infant rickets is still a threat to the premature infant who survives the neonatal period.

Various authors from time to time have stressed one or all of the following etiologic factors for the prevalence and severity of rickets in the premature infant: (1) the relatively rapid growth of the premature as compared with the normal full-term infant; (2) the tendency of the premature infant to anemia; (3) the fact that its size and frailty necessitate its remaining indoors throughout the early weeks and months, often away from sunlight, and (4) a deficient store of calcium at birth. Abt [1] said: "In spite of everything you do with prematures, if they are viable, they are likely to develop rickets," and, again, "All premature infants have a marked predisposition to rickets. . . . they grow rapidly, and rapidly growing babies are apt to become rachitic." Eliot [2] stated, in 1925, that it was perhaps impossible to prevent rickets entirely in rapidly growing infants; that rickets is intimately associated with growth and appears at the period of most active growth, that is, during the first four months of life; that rickets is prone to develop in premature babies who grow exceedingly rapidly, and finally that a slight degree of early rickets is almost universal in the climate and state of society existing in the United States. Jundell [3] revived Glisson's idea that rickets is in part due to overeating, and Hess [4] stated that overfeeding leads to a definite clinical type of rickets: that found in the

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1. Abt, I. A.: Prematurity and Rickets, Proc. Inter-State Post-Grad. M. A. North America **6**:224 (Oct.) 1930.

2. Eliot, M. M.: The Control of Rickets, J. A. M. A. **85**:656 (Aug. 29) 1925.

3. Jundell, I.: Pathogenesis and Treatment of Rickets, Hygiea **83**:753 (Nov.) 1921.

4. Hess, A. F.: Rickets, Osteomalacia and Tetany, Philadelphia, Lea & Febiger, 1929.

overweight, well nourished, bow-legged baby. He also said that rickets is one of the greatest dangers associated with overfeeding, and that rapid growth following periods of delayed growth is likely to be accompanied by the most active rickets. Park,[5] in an earlier article on the etiology of rickets, stated that the premature infant differs from the full-term infant in the following ways: First, it has a lower basal metabolism. Second, it metabolizes fat poorly. Third, it has a deficient deposit of calcium. He believed that the calcium deficiency might be a possible explanation of the rickets, but thought that as susceptibility to rickets varies with age and culminates in the premature infant, the immaturity of the organism and its tremendous impetus for growth are the important underlying factors. Ylppö [6] used this explanation of the tendency of anemia to develop in the premature infant. Baumann,[7] in 1928, studied the association of anemia and rickets in premature infants and concluded that there was a summation effect of the physiologic anemia of prematurity added to the anemia which he considered was usually found in rachitic infants. He felt that the degree of anemia was in direct proportion to the degree of rickets present. Park [5] spoke of anemia and rickets in the premature infant as sister conditions, each an expression of the inability of the organism to discharge its functions properly when thrown on its own resources. He also drew an analogy between the premature infant and the experimental animal, in that rickets did not tend to develop in animals which grew poorly, but large deposits of lime salts were made at the junction of the cartilage and shaft. Malnourished infants do not tend to become anemic, nor do they show marked rickets. From a study of anemia in the premature infant, reported in a previous paper,[8] it is not our impression that anemia has any appreciable influence on the development of rickets, or rickets on the development of anemia in infants born before term.

Appreciation of the susceptibility of the premature infant to the development of rickets led us, in 1930, to begin an investigation of the protective powers of viosterol. The literature up to that time contained only occasional references to its application to premature infants, and those references were included in clinical reports of the prophylactic and therapeutic effect on animals and rachitic infants of all ages and types. At the beginning of the study the question of dosage was a real one, in view of the inadequacy of definite knowledge concerning the pro-

5. Park, E. A.: The Etiology of Rickets, Physiol. Rev. **3**:106 (Jan.) 1923.

6. Ylppö, A.: Zur Physiologie, Klinik, und zum Schicksal der Frühgeborenen, Ztschr. f. Kinderh. **24**:1 (Dec.) 1919.

7. Baumann, T.: Zur Frage der Anämie bei Rachitis, Monatschr. f. Kinderh. **39**:193 (June) 1928.

8. Merritt, K. K., and Davidson, L. T.: The Blood During the First Year of Life. The Anemia of Prematurity, Am. J. Dis. Child. **47**:261 (Feb.) 1934.

tective and therapeutic potency of viosterol. Various German investigators had reported hypercalcemia, arteriosclerosis and toxic effects from the use of viosterol in animals, but the doses which they used were many times greater than those thought to be necessary for adequate protection of the human infant.

Alfred Hess and Lewis [9] in 1928 said, "As yet we have not sufficient clinical experience with irradiated ergosterol to define its proper dosage. Furthermore, the various preparations cannot be evaluated as they have not yet been assayed on the basis of curative units (rat) which they contain. Amounts now recommended and employed are unnecessarily high." Jundell [10] used moderate doses of viosterol in 6 premature infants, and asserted that he had prevented the rachitic fall of inorganic phosphorus in the blood and changes in the skeleton, as shown by roentgenograms. In 1929 Alfred Hess and his collaborators [11] recommended from 8 to 10 drops of viosterol 100 D a day as a prophylactic dosage for infants growing at a normal rate and for premature and rapidly growing infants a dose of at least 15 drops a day. With these doses he believed that neither toxic effects nor hypercalcemia need be feared. In 1930 Hess and his co-workers [12] raised the dosage to 30 drops as they had failed to protect 10 of 60 normal infants from rickets on a dosage of from 10 to 20 drops a day of viosterol 100 D. They reiterated the belief that premature infants require an extra amount of viosterol, but stated no definite dosage. Julius Hess and his associates,[13] in the same year, gave 63 full-term infants 10 drops a day of viosterol 100 D. None showed evidence of rickets on roentgenologic examination or blood chemistry. Mild clinical rickets was evident in 6 without roentgen examination or tests for changes in the blood. In another group given larger doses they found that no infant receiving more than 10 drops a day of viosterol 100 D showed clinical, roentgenographic or chemical evidence of rickets. They therefore concluded that 10 drops of viosterol 100 D a day was the minimal prophylactic dose for normal infants, and advised starting its administration in the first weeks of life. May,[14] in 1931, reported the use of viosterol 100 D in

9. Hess, A. F., and Lewis, J. M.: Clinical Experience with Irradiated Ergosterol, J. A. M. A. **91**:783 (Sept. 15) 1928.

10. Jundell, I.: Klinische Versuche über Ersatzmittel für Lebertran bei der Profylaxe der Rachitis, Acta pædiat. **8**:341 (Dec.) 1928.

11. Hess, A. F.; Lewis, J. M., and Rivkin, H.: Status of the Therapeutics of Irradiated Ergosterol, J. A. M. A. **93**:661 (Aug. 31) 1929.

12. Hess, A. F.; Lewis, J. M., and Rivkin, H.: Newer Aspects of the Therapeutics of Viosterol, J. A. M. A. **94**:1885 (June 14) 1930.

13. Hess, J. H.; Poncher, H. G.; Dale, M. L., and Klein, R. L.: Viosterol (Irradiated Ergosterol): Prophylactic and Therapeutic Dosage, J. A. M. A. **95**: 316 (Aug. 2) 1930.

14. May, E. W.: Prevention of Rickets in the Premature Infant by the Use of Viosterol 100D, J. A. M. A. **96**:1376 (April 25) 1931.

32 premature infants from birth for varying periods, from three weeks to five months. Ten infants received a "minimal dose" of 36 drops a day; 22 infants received a "maximal dose" of 60 drops a day. He noted a definite improvement in weight, general well-being, percentage of hemoglobin, calcium-phosphorus product and development of bone in those infants who received an "adequate" dose daily as compared with those whose mothers were indifferent in following instructions. He noted a rise in the phosphorus level and a fall in the calcium level of the blood during the fourth week of treatment, after which both returned to normal levels. Roentgenograms of the long bones and the chest were taken at intervals of two weeks, but the findings were not reported. May recommended viosterol 100 D in a dosage of from 30 to 60 drops a day as effective in the prevention of rickets in the premature infant.

Viosterol was used throughout this study. Viosterol 250 D was used in the majority of cases, but 2 patients received viosterol 100 D for two months prior to the time that viosterol 250 D was put on the market. Administration of viosterol was begun as soon after birth as it was apparent that the infant was viable—usually about the seventh day. The initial dose was 2 drops a day for a week, then 4 drops per kilogram of body weight daily until the infant weighed 2,250 Gm., after which the dose was maintained at 20 drops a day to the fifth or sixth month. These doses were well tolerated even in the early weeks of life, and caused no digestive disturbances. The dose was given by dropper directly into the mouth to prevent the loss which occurs when it is given in the formula or with orange juice. Untreated infants, used as controls, received a mixture of equal parts of cotton seed oil and liquid petrolatum in similar dosage up to 5 or 6 months of age before being given intensive antirachitic therapy.

## MATERIAL AND METHOD

All the infants included in this study were delivered in the Sloane Hospital for Women and were sent at once to the nursery for premature infants where they remained under our close daily observation for varying periods until they reached a weight of 2,250 Gm. They were then discharged to a follow-up clinic, where they were seen twice a month for the first six months of life and once a month thereafter. All clinical observations and records were made by one or the other of us. Frequent visits were made to each home by a social worker to make sure that the instructions given at the clinic were carried out. All the infants received breast milk exclusively from the first day of life for varying periods up to four weeks, after which a formula was gradually introduced if breast feeding was not to continue. The formulas consisted of evaporated milk, boiled whole milk or Dryco, in the order of frequency named, with cane sugar and Karo syrup as the predominating sugars. The caloric intake was kept at approximately 130 calories per kilogram of body weight. This was found to be sufficient for the appetite of the average healthy premature infant and produced a satisfactory gain in weight. No attempt was made to increase the calories to induce a rapid gain. Cereal was

added at the fourth or fifth month, vegetable and egg yolk at the fifth or sixth and stewed fruit at the sixth or seventh month. Mothers were instructed to keep their infants outdoors in the direct sunlight as much as possible, but they were not instructed to give sun-baths without clothing.

The values for the serum calcium and inorganic phosphorus were determined at the ages of approximately 1 week, 6 weeks, 3 months and 5 or 6 months.[15] For a few of the smaller premature infants the initial chemical examination was not made before the fourteenth to the twenty-first day. Blood was obtained from the median basilic vein except in occasional instances when it was taken from the external or internal jugular vein. The serum calcium content was determined by the Clark-Collip[16] modification of the Kramer and Tisdall[17] method, using 1 cc. of serum. The value for inorganic phosphorus was determined by the method of Benedict and Theis.[18]

Roentgenograms of the long bones were taken at the age of 6 weeks, 3 months and 5 months. These roentgenograms were compared with the clinical findings and with the chemical determinations in an attempt to detect by one or the other of these means the earliest evidence of the development of rickets.

## I. CLINICAL CONSIDERATIONS

It is a well known fact that the clinical manifestations of rickets vary considerably. In some infants a square head with enlarged bosses is a prominent feature, in others a marked enlargement at the costochondral junctions shows earliest, while in some, with moderately advanced rickets, no other involvement than enlarged epiphyses is evident. Hess and Unger[19] stated that sweating of the head, delayed eruption of the teeth, poor muscle tone and inability to sit or stand at the normal age are all unreliable as diagnostic signs of rickets. They believed that beading of the ribs is the most reliable sign. Eliot[2] made a positive diagnosis of rickets by any two of the following findings: (1) enlarged costochondral junctions, (2) enlarged radial epiphyses, (3) prominent bosses, (4) craniotabes and (5) Harrison's groove. In a recent article Eliot[20] included nutrition, motor development, the

15. All chemical determinations were made by Dr. Ruth C. Sullivan and Miss Zdenka Wolf.

16. Clark, E. P., and Collip, J. B.: A Study of the Tisdall Method for the Determination of Blood Serum Calcium with a Suggested Modification, J. Biol. Chem. **63**:461 (March) 1925.

17. Kramer, B., and Tisdall, F. F.: A Simple Technique for the Determination of Calcium and Magnesium in Small Amounts of Serum, J. Biol. Chem. **47**:475 (Aug.) 1921.

18. Benedict, S. R., and Theis, R. C.: A Modification of the Molybdic Method for the Determination of Inorganic Phosphorus in Serum, J. Biol. Chem. **61**:63 (Aug.) 1924.

19. Hess, A. F., and Unger, L. J.: Infantile Rickets: The Significance of Clinical Radiographic and Chemical Examinations in Its Diagnosis and Incidence, Am. J. Dis. Child. **24**:327 (Oct.) 1922.

20. Eliot, M. M.; Nelson, E. M.; Souther, S. P., and Cary, M. K.: The Value of Salmon Oil in the Treatment of Infantile Rickets, J. A. M. A. **99**:1075 (Sept. 24) 1932.

number of teeth erupted and the size of the anterior fontanel among the clinical criteria. Dalyell and MacKay [21] stated that craniotabes at the age of 3 months, beading of the ribs at from 5 to 6 months and bossing are the most reliable early signs of rickets. They believed that epiphyseal enlargement is a late sign that may persist after activity has ceased; that some enlargement of the wrists and ankles is normal at the end of the first year; that the large fontanel is only confirmatory and may often be misleading, and that a thoracic deformity is often a secondary sign. Pallor, sweating, poor muscle tone, abdominal distention and general retardation of growth can be only suggestive in early rickets. They believed that splenic enlargement is not a diagnostic sign.

The question of craniotabes has aroused considerable discussion. Jundell [22] attributed the first description of this condition to Elsässer,[23] who regarded it as a manifestation of infantile rickets. In 1908 Wieland [24] differentiated rachitic craniotabes from physiologic craniotabes which occurred in subjects who showed no other signs of rickets and which was not influenced by antirachitic treatment. Jundell,[22] in a series of 129 infants who received intensive antirachitic therapy throughout the first two years of life and 79 infants who received no antirachitic therapy, found that in general those infants showing craniotabes did not exhibit other signs of rickets any more often than those who were free from craniotabes. He concluded that craniotabes should be considered not as a rachitic phenomenon but rather as physiologic hypoplasia. Alfred Hess [4] asserted that the presence or absence of craniotabes is of no diagnostic significance, and that it is difficult to differentiate it in the early months from the cranial softening of the new-born which he called "congenital bone defect." Dunham,[25] in reporting a case of rickets in an infant 34 days of age, stated that craniotabes which develops under observation or is widespread in the region of the lambdoidal sutures justifies the diagnosis of rickets. Huenekens [26] said that congenital craniotabes disappears in the first two

21. Dalyell, E. J., and MacKay, H. M. M.: Notes on the Clinical Signs of Infantile Rickets: Studies of Rickets in Vienna, Medical Research Council, London, His Majesty's Stationery Office, 1923.

22. Jundell, I.: The Clinical Significance of Craniotabes, Acta pædiat. **12**:1 (Sept.) 1931.

23. Elsässer, C. L.: Der weiche Hinterkopf, Stuttgart, J. G. Cotta'scher Verlag, 1843.

24. Wieland, E.: Ueber sogenannte angeborene und über frühzeitig erworbene Rachitis. Klinische und anatomische Untersuchungen, Jahrb. f. Kinderh. **67**:675 (June) 1908.

25. Dunham, E. C.: Rickets in an Infant of Thirty-Four Days, Am. J. Dis. Child. **26**:155 (Aug.) 1923.

26. Huenekens, E. J.: Rickets with Especial Reference to Premature Infants, Journal-Lancet **37**:804 (Dec. 15) 1917.

months, while rachitic craniotabes increases up to the age of 6 months. Eliot,[2] in dealing with definitely rachitic infants, found that when craniotabes was marked, the diagnosis of rickets could be made by that alone, in the absence of other signs, and that in all cases in which craniotabes was present, the diagnosis of rickets was corroborated by roentgenograms. There is now a general agreement that craniotabes may be of two types: the so-called "physiologic" type, occurring at the margins of the sutures of the cranial bones and often observed during the first two or three months, and a second type which involves the center of the cranial bones and is considered pathognomonic of rickets only after the third month.

Of the various criteria which have been suggested for the clinical estimation of the presence of rickets we have used the following as being most reliable: (1) enlarged bosses, (2) enlarged costochondral junctions, (3) enlarged epiphyses and (4) craniotabes. The prevalence and severity of those criteria in the two groups of premature infants—1 group untreated, the other receiving early and continued antirachitic therapy in the form of viosterol—are shown in tables 1 and 2, respectively.

In the infants who received no antirachitic therapy there was no regularity in the order of the appearance of any of the clinical criteria, nor can it be said that any one sign predominated as the evidence of developing rickets increased.

Those infants who received antirachitic therapy were almost entirely free from clinical signs of rickets while receiving the dosage indicated, and showed no deviation from the normal levels for the serum calcium and inorganic phosphorus, although there was in almost all, as will be demonstrated later, some roentgenologic evidence of a definite rachitic involvement.

The premature infant is generally considered peculiarly subject to craniotabes, but we have not found this to be true. In only 10 of the 22 infants not receiving antirachitic therapy was craniotabes of even a slight degree noted at any time. In some cases it was present when other signs of rickets were entirely absent. In others it was conspicuously absent even when rickets was definitely present elsewhere.

## II. CHEMICAL CONSIDERATIONS

A deficient store of calcium at birth and an inability to metabolize calcium adequately through the early months have both been considered as etiologic factors in the susceptibility of the premature infant to rickets. Huenekens [26] stated that the fetus acquires two thirds of its mineral content in the last three months of fetal life, and therefore, the more premature the infant, the more deficient it is in calcium and

TABLE 1.—*Observations on Twenty-Two Premature Infants Receiving Viosterol Only After the Development of Definite Rickets*

| Race; Weight and Length at Birth | Date | Age | Clinical Data | | | | | | Blood Chemistry | | | Roentgenograms | | Therapy Began After Definite Rickets | Comment |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Percentage Increase Over Birth Weight | Rosary | Groove | Enlarged Epiphyses | Cranial Bosses | Craniotabes | Calcium, Mg. per 100 Cc. of Serum | Inorganic Phosphorus, Mg. per 100 Cc. of Serum | Calcium-Phosphorus Product | Degree and Stage of Rickets | Comment | | |
| Case 1 | 8/ 7 | 4 days | ... | .. | .. | .. | .. | .. | 11.2 | 5.8 | 65 | | | | |
| white; | 9/25 | 6 wk. | 62 | .. | .. | .. | .. | + | 11.0 | 5.6 | 62 | A1 O2* | Distal end of ulna | | |
| 2,130 Gm.; | 11/ 6 | 3 mo. | 152 | + | .. | .. | .. | ++ | 11.4 | 6.8 | 77 | A1 O2 | Possibly slight healing | | |
| 44 cm. | 1/29 | 6 mo. | 229 | ++ | + | .. | .. | ++ | 11.6 | 5.4 | 63 | B1 O1 | Definite mild rickets with healing | 6 months; cod liver oil | Rapidly growing infant |
| Case 2 | 7/24 | 5 days | ... | .. | .. | .. | .. | .. | 10.8 | 7.5 | 80 | | | | |
| white; | 9/ 4 | 6 wk. | 55 | .. | .. | .. | .. | .. | 11.2 | 6.5 | 73 | | | | |
| 2,240 Gm.; | 10/30 | 3½ mo. | 123 | + | + | + | + | ++ | 10.6 | 7.5 | 83 | A1 O1 | Distal end of ulna and radius, proximal end of ulna | | |
| 44.5 cm. | 12/11 | 5 mo. | 191 | + | ++ | + | ++ | ++ | 11.2 | 6.0 | 67 | B1 O1 | Mottled medulla, slight flaring | 5 months; viosterol 250 D | |
| Case 3 | 10/23 | 2 days | ... | .. | .. | .. | .. | .. | 10.2 | | | | | | |
| Negro; | 12/ 4 | 6 wk. | 54 | .. | + | .. | .. | .. | 10.6 | 5.3 | 56 | A1 O1 | Proximal end of ulna, distal end of shaft laterally | | |
| 2,380 Gm.; 44.5 cm. | 1/22 | 3 mo. | 104 | .. | + | .. | + | + | 7.4 | 4.6 | 34 | A2 O2 | Flaring, cupping, spurring | | |
| | 3/11 | 5 mo. | 133 | ++ | + | +++ | ++ | ++ | 8.6 | 3.4 | 29 | A3 O3 | Distal end of humerus | 5 months; cod liver oil and viosterol 100 D | Latent tetany; Chvostek sign; peroneals ± |
| Case 4 | 7/ 3 | 6 wk. | 86 | .. | .. | .. | .. | .. | 11.2 | 6.1 | 68 | | | | |
| white; | 8/28 | 3 mo. | 124 | ++ | + | .. | +++ | .. | 12.6 | 6.6 | 83 | ..... | Doubtful rickets with summer healing | ..... | Acute intestinal indigestion |
| 2,070 Gm.; 46 cm. | 10/20 | 5 mo. | 148 | + | .. | .. | ++ | .. | 11.2 | 6.2 | 69 | A1 O2 | Calcification in primary zone less dense; osteoporosis of shafts | 5 months; viosterol 250 D | |
| Case 5 | 7/31 | 3 days | ... | .. | .. | .. | .. | .. | 10.2 | 8.0 | 82 | | | | |
| white; | 9/11 | 6 wk. | 71 | .. | .. | .. | .. | .. | 11.2 | 6.5 | 73 | | | | |
| 2,130 Gm.; | 10/23 | 3 mo. | 114 | .. | .. | .. | .. | .. | 9.6 | 7.0 | 67 | ..... | Heavy bone, no rickets | | |
| 42.5 cm. | 12/31 | 5 mo. | 171 | + | ++ | .. | ++ | .. | 12.4 | 5.2 | 64 | A1 O2 | Cupping of distal end of ulna; irregular calcification in primary zone; little flaring | 5 months; cod liver oil and viosterol 100 D | |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case 6 | 7/ 3 | 12 days | ... | .. | .. | .. | .. | .. | 12.6 | 6.4 | 81 | ..... | ..... | ..... | Twin |
| white; | 7/31 | 6 wk. | 44 | .. | .. | .. | .. | .. | 10.8 | 5.1 | 55 | | | | |
| 1,620 Gm.; | 9/ 6 | 3 mo. | 131 | | | | | | | | | | | | |
| 41.5 cm. | 10/30 | 4½ mo. | 160 | .. | .. | .. | .. | .. | 10.8 | 6.2 | 67 | C4 O3 | Marked rickets with marked summer healing | None | |
| Case 7 | 10/23 | 13 days | ... | .. | .. | .. | .. | .. | 10.6 | 6.9 | 73 | | | | |
| Negro; | 12/ 4 | 6 wk. | 78 | .. | .. | .. | .. | .. | .... | ... | .. | A1 O2 | Furring of proximal end of ulna | | |
| 1,840 Gm.; | | | | | | | | | | | | | | | |
| 42.5 cm. | 1/15 | 3½ mo. | 139 | + | .. | .. | .. | ++ | 8.2 | 4.7 | 39 | | | | |
| | 3/ 4 | 5 mo. | 200 | ++ | +++ | ++ | ++ | ++ | 7.8 | 5.1 | 40 | B4 O4 | Periosteum of femur filling in very slightly; rickets still active | 5 months; viosterol 250 D | |
| Case 8 | 1/22 | 18 days | ... | .. | .. | .. | .. | .. | 10.8 | 7.2 | 78 | | | | |
| white; | 2/26 | 7 wk. | 92 | .. | .. | .. | .. | + | 7.6 | 7.1 | 54 | A1 O1 | Thin bones; slight cupping of distal end of ulna; furring of proximal end of ulna | | |
| 1,190 Gm.; | | | | | | | | | | | | | | | |
| 39 cm. | | | | | | | | | | | | | | | |
| | 4/ 1 | 3 mo. | 167 | .. | + | .. | + | ++ | 7.6 | 6.4 | 49 | A2 O3 | ..... | 3 months; viosterol 250 D | Latent tetany; Chvostek sign + |
| | 6/ 3 | 5 mo. | 275 | | | | | | | | | | | | |
| Case 9 | 12/24 | 9 days | ... | .. | .. | .. | .. | .. | 10.4 | 7.3 | 76 | | | | |
| white; | 2/ 5 | 7 wk. | 48 | .. | .. | .. | .. | + | 8.0 | 5.4 | 43 | A1 O1 | Proximal end of ulna ragged and hazy | | |
| 2,300 Gm.; | | | | | | | | | | | | | | | |
| 44.5 cm. | 3/25 | 3 mo. | 113 | .. | .. | + | + | ++ | 10.4 | 5.7 | 59 | A2 O2 | Advancing rickets | | |
| | 5/20 | 5 mo. | 187 | .. | + | .. | + | .. | .... | ... | .. | ..... | ..... | 5¼ months; cod liver oil | |
| Case 10 | 10/12 | 6 wk. | 62 | | | | | | | | | | | | |
| white; | 10/30 | 2 mo. | ... | .. | .. | .. | .. | .. | 11.2 | 6.3 | 61 | ..... | Doubtful rickets | | |
| 2,130 Gm.; | 11/27 | 3 mo. | 124 | .. | + | .. | .. | .. | 11.4 | 6.2 | 71 | B1 O1 | Slight rickets with beginning healing | ..... | Cod liver oil 2 cc. 4 times a day for 1 week |
| 47 cm. | | | | | | | | | | | | | | | |
| | 2/ 5 | 5 mo. | 205 | .. | .. | .. | .. | .. | 9.8 | 6.2 | 61 | B1 O1 | ..... | 7 months; cod liver oil and viosterol 100 D | |
| Case 11 | 8/21 | 4 days | ... | .. | .. | .. | .. | .. | 8.6 | 6.0 | 52 | | | | |
| Negro; | 10/ 9 | 7 wk. | 71 | .. | .. | .. | .. | .. | 9.4 | 5.1 | 48 | A1 O2 | Thickening of cortex | | |
| 1,670 Gm.; | 11/20 | 3 mo. | 141 | .. | + | .. | .. | + | 7.2 | 6.3 | 45 | A3 O4 | Marked furring of proximal end of ulna; legs markedly involved | 3 months; viosterol 250 D | Very flabby infant showing fairly rapid growth |
| 41.5 cm. | | | | | | | | | | | | | | | |
| | 1/15 | 5 mo. | 218 | .. | .. | .. | .. | .. | .... | ... | .. | B3 O3 | Marked periostitis; progression with healing | | |

* For the purpose of clarity and brevity we have used the letters A, B, C as follows: A, active progressive rickets without evidence of healing; B, the rachitic process in balance, that is, with evidence of healing in the presence of continued activity, and C, healed rickets without evidence of activity. Osteoporosis is represented by O. The degree of the rachitic involvement and osteoporosis is graded by the numbers 1, slight; 2, moderate; 3, marked, and 4, severe involvement. Negative clinical findings are represented by blank spaces rather than by zeros. Positive clinical findings are represented in the order of severity, on the scale of +, ++, +++ and ++++.

TABLE 1.—*Observations on Twenty-Two Premature Infants Receiving Viosterol Only After the Development of Definite Rickets—Continued*

| Race; Weight and Length at Birth | Date | Age | Clinical Data: Percentage Increase Over Birth Weight | Rosary | Groove | Enlarged Epiphyses | Cranial Bosses | Craniotabes | Blood Chemistry: Calcium, Mg. per 100 Cc. of Serum | Inorganic Phosphorus, Mg. per 100 Cc. of Serum | Calcium-Phosphorus Product | Roentgenograms: Degree and Stage of Rickets | Roentgenograms: Comment | Therapy Began After Definite Rickets | Comment |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case 12 white: 2,010 Gm.; 44 cm. | 8/21 | 6 days | ... | .. | .. | .. | .. | .. | 11.6 | 4.7 | 54 | ..... | ..... | ..... | Thrush |
| | 10/ 9 | 7 wk. | 55 | .. | .. | .. | .. | .. | 11.2 | 5.4 | 60 | ..... | No rickets | | |
| | 11/20 | 3 mo. | 115 | .. | + | .. | .. | .. | 10.4 | 4.5 | 47 | A1 O3 | Fraying distal end of ulna; marked osteoporosis | | |
| | 1/15 | 5 mo. | 195 | ++ | + | .. | ++ | + | .... | ... | .. | ..... | ..... | ..... | Acute intestinal indigestion |
| | 2/19 | 6 mo. | .... | ++ | .. | + | ++ | .. | 10.0 | 4.5 | 45 | B2 O3 | Moderate rickets with some healing | 6 months; cod liver oil | |
| Case 13 Negro; 1,670 Gm.; 41.5 cm. | 7/31 | 10 days | ... | .. | .. | .. | .. | .. | 11.4 | 6.4 | 63 | | | | |
| | 8/28 | 6 wk. | 65 | .. | .. | .. | .. | ++ | 8.2 | 6.2 | 51 | | | | |
| | 10/23 | 3 mo. | 118 | + | + | + | .. | .. | 8.0 | 5.7 | 46 | A3 O3 | Marked periostitis | | |
| | 12/15 | 5 mo. | 218 | .. | .. | .. | .. | .. | .... | ... | .. | B3 O2 | Periostitis with beginning healing | 4 months; viosterol 250 D | |
| Case 14 Negro; 2,070 Gm.: 44.5 cm. | 9/25 | 8 days | ... | .. | .. | .. | .. | .. | 9.6 | 5.9 | 57 | | | | |
| | 11/12 | 7 wk. | 33 | .. | .. | .. | .. | .. | 6.6 | 4.5 | 30 | A1 O2 | Distal end of humerus, proximal end of fibula | ..... | No signs of tetany |
| | 1/ 7 | 3½ mo. | 90 | +++ | ++ | + | ++ | .. | 6.2 | 4.2 | 26 | A4 O4 | Legs more involved than arms; costochondral junctions very ragged | 3½ months; viosterol 250 D | Slightly hypertonic; no Chvostek or other signs of tetany |
| | 3/15 | 5 mo. | 132 | | | | | | | | | | | | |
| | 4/ 5 | 6 mo. | ... | .. | .. | .. | .. | .. | .... | ... | .. | C4 O1 | Very wide metaphysis in arms | | |
| Case 15 white; 2,350 Gm. 45 cm. | 6/12 | 4 days | ... | .. | .. | .. | .. | .. | 9.8 | 5.0 | 49 | | | | |
| | 7/17 | 6 wk. | 63 | .. | + | .. | .. | + | 11.0 | 5.7 | 63 | | | | |
| | 9/ 4 | 3 mo. | 117 | .. | + | .. | .. | + | 10.8 | 5.9 | 64 | B1 O2 | Calcification in primary zone; slight summer healing | | |
| | 10/31 | 5 mo. | 204 | .. | + | .. | + | + | .... | ... | .. | B1 O3 | Healing and activity | 5 months; cod liver oil and viosterol 100 D | |
| Case 16 white; 2,180 Gm. 44 cm. | 7/10 | 9 days | ... | .. | .. | .. | .. | .. | 9.8 | 5.5 | 54 | | | | |
| | 10/ 9 | 3 mo. | 150 | .. | .. | .. | .. | .. | 12.0 | 5.5 | 66 | | | | |
| | 12/11 | 5 mo. | 209 | + | .. | .. | + | .. | 11.0 | 6.8 | 75 | B1 O3 | Legs showed osteoporosis more than arms | 8 months; | |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case 17 | 12/11 | 6 days | ... | .. | .. | .. | .. | .. | 10.0 | 4.7 | 47 | | | |
| white; | 1/15 | 6 wk. | 73 | .. | + | .. | .. | + | 10.6 | 5.0 | 53 | ..... | Doubtful rickets | ..... | Papular eczema |
| 2,210 Gm.; | 3/11 | 3 mo. | 127 | + | .. | .. | +++ | +++ | 10.4 | 5.0 | 52 | A1 O2 | Furring of the proximal end of ulna | | |
| 45 cm. | 5/ 6 | 5 mo. | 164 | ++ | .. | .. | +++ | + | .... | ... | .. | B1 O2 | Healing rickets of mild degree | 6 months; viosterol 250 D | |
| Case 18 | 7/10 | 3 days | ... | .. | .. | .. | .. | .. | 11.0 | 7.4 | 81 | | | | |
| white; | 8/21 | 6 wk. | 52 | .. | .. | .. | .. | .. | 8.8 | 6.7 | 59 | A2 O1 | Marked periostitis in the proximal end of ulna with furring | | |
| 2,130 Gm.; 44.5 cm. | 10/ 2 | 3 mo. | 105 | .. | .. | .. | .. | + | 11.6 | 6.2 | 62 | | | | |
| | 12/15 | 5½ mo. | 205 | .. | ++ | + | +++ | .. | 10.2 | 5.9 | 60 | B2 O2 | Beginning filling in of periosteum | 7 months; cod liver oil | |
| Case 19 | 10/23 | 5 days | ... | .. | .. | .. | .. | .. | 11.4 | 6.1 | 70 | | | | |
| white; | 12/ 4 | 7 wk. | 44 | .. | .. | .. | .. | .. | 10.8 | 6.2 | 67 | A1 O0 | Furring of proximal end of ulna | | |
| 2,660 Gm.; 45 cm. | 1/22 | 3 mo. | 85 | .. | + | .. | .. | + | 12.6 | 5.3 | 67 | A2 O1 | Increased raggedness of proximal end of ulna | ..... | Acute bronchitis |
| | 4/ 1 | 4½ mo. | 122 | .. | + | .. | + | ++ | 11.8 | 5.8 | 68 | A3 O3 | Thickened cortex | 5½ months; viosterol 250 D | |
| Case 20 | 8/17 | 9 days | ... | .. | .. | .. | .. | .. | 10.4 | 6.7 | 70 | | | | |
| Negro; | 9/18 | 6 wk. | 42 | .. | .. | .. | + | .. | 10.2 | 6.0 | 61 | A1 O1 | Periostitis of distal end of femur and inner curve of tibia | | |
| 2,380 Gm.; 46 cm. | 11/20 | 3½ mo. | 79 | ++ | + | .. | +++ | .. | 9.0 | 4.6 | 41 | A4 O4 | Florid rickets | 4 months; viosterol 250 D | |
| | 1/ 4 | 5 mo. | 163 | + | .. | .. | ++ | .. | .... | ... | .. | B4 O4 | Wide metaphysis, coarse trabeculae; marked osteoporosis | | |
| Case 21 | 10/23 | 6 days | ... | .. | .. | .. | .. | .. | 9.8 | 6.6 | 65 | | | | |
| Negro; | 11/20 | 5 wk. | 32 | .. | .. | .. | .. | + | 11.4 | 6.1 | 70 | ..... | Doubtful rickets | | |
| 2,180 Gm.; | 1/22 | 3 mo. | 64 | .. | + | .. | .. | ++ | 8.6 | 6.0 | 52 | A1 O1 | | | |
| 45.5 cm. | 3/18 | 5 mo. | 109 | ++ | .. | ++ | ++ | ++++ | 7.4 | 4.6 | 34 | A3 O3 | Fraying and cupping of distal end of ulna and radius | 5 months; viosterol 250 D | Markedly hypertonic infant; Chvostek sign |
| | 4/29 | 6½ mo. | ... | .. | .. | .. | .. | .. | .... | ... | .. | B3 O3 | | | |
| Case 22 | 12/31 | 9 days | ... | .. | .. | .. | .. | .. | 10.0 | 5.8 | 58 | | | | |
| Negro; | 2/ 5 | 6 wk. | 68 | .. | .. | .. | .. | + | 7.8 | 5.3 | 41 | A1 O1 | Periostitis of distal end of humerus | ..... | Seborrheic eczema; had cod liver oil 4 times a day for 1 week |
| 1,870 Gm.; 44 cm. | 4/ 1 | 3½ mo. | 105 | ++ | +++ | ++ | .. | +++ | 9.4 | 4.4 | 41 | A4 O4 | Florid rickets (winter infant) | 3½ months; viosterol 250 D | |
| | 5/20 | 5 mo. | 168 | .. | .. | .. | .. | .. | 8.8 | 4.0 | 35 | | | | |

* For the purpose of clarity and brevity we have used the letters A, B, C as follows: A, active progressive rickets without evidence of healing; B, the rachitic process in balance, that is, with evidence of healing in the presence of continued activity, and C, healed rickets without evidence of activity. Osteoporosis is represented by O. The degree of the rachitic involvement and osteoporosis is graded by the numbers 1, slight; 2, moderate; 3, marked, and 4, severe involvement. Negative clinical findings are represented by blank spaces rather than by zeros. Positive clinical findings are represented in the order of severity, on the scale of +, ++, +++ and ++++.

TABLE 2.—*Observations on Thirteen Premature Infants Receiving Viosterol Therapy Soon After Birth*

| Race; Weight and Length at Birth | Date | Age | Clinical Data: Percentage Increase Over Birth Weight | Rosary | Groove | Enlarged Epiphyses | Cranial Bosses | Craniotabes | Blood Chemistry: Calcium, Mg. per 100 Cc. of Serum | Inorganic Phosphorus, Mg. per 100 Cc. of Serum | Calcium-Phosphorus Product | Roentgenograms: Degree and Stage of Rickets | Roentgenograms: Comment | Therapy Begun | Comment |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case 1 | .... | ..... | ... | .. | .. | .. | .. | .. | .... | ... | .. | ..... | ..... | Fourteenth day | Cerebral hemorrhage at birth, with transfusion |
| Negro; | | | | | | | | | | | | | | | |
| 2,155 Gm.; | 1/23 | 6 wk. | 64 | .. | .. | .. | .. | .. | 11.6 | 5.0 | 58 | | | | |
| 44.6 cm. | 3/27 | 3 mo. | 145 | .. | .. | .. | .. | .. | 10.8 | 6.8 | 73 | B1 O0* | Cupping and flaring of distal end of ulna | | |
| | 5/12 | 5 mo. | 232 | .. | .. | .. | .. | .. | 12.0 | 5.6 | 67 | C1 O1 | Previous changes persist though rickets are healed | | |
| Case 2 | 6/ 6 | 12 days | ... | .. | .. | .. | .. | .. | 11.8 | 5.0 | 59 | ..... | ..... | Twelfth day | |
| white; | 8/22 | 3 mo. | 118 | .. | .. | .. | .. | .. | .... | 5.9 | | | | | |
| 2,180 Gm.; | 11/ 7 | 5½ mo. | 164 | .. | .. | .. | .. | .. | 11.2 | 5.1 | 57 | C1 O1 | Very mild healed rickets in distal end of ulna | ..... | Acute intestinal intoxication, with otitis media |
| 44.7 cm. | | | | | | | | | | | | | | | |
| Case 3 | .... | ..... | ... | .. | .. | .. | .. | .. | .... | ... | .. | ..... | ..... | Twenty-first day; viosterol 100 D | |
| white; | | | | | | | | | | | | | | | |
| 1,930 Gm.; | | | | | | | | | | | | | | | |
| 45 cm. | 6/13 | 6 wk. | 42 | .. | .. | .. | .. | .. | 8.6 | 6.1 | 52 | ..... | ..... | ..... | Thrush |
| | 7/25 | 3 mo. | 126 | .. | .. | .. | .. | .. | 11.3 | 6.2 | 70 | | | | |
| | 9/24 | 5 mo. | 200 | .. | + | .. | .. | .. | 11.3 | 6.4 | 72 | C1 O0 | Very mild healed rickets in distal end of radius | | |
| Case 4 | 7/ 3 | 13 days | ... | .. | .. | .. | .. | .. | 10.2 | 6.8 | 69 | ..... | ..... | Fifteenth day | Twin |
| white; | 7/31 | 6 wk. | 57 | .. | .. | .. | .. | .. | 11.2 | 6.0 | 67 | A2 O2 | Proximal and distal end of ulna | | |
| 1,360 Gm.; | | | | | | | | | | | | | | | |
| 40 cm. | 9/20 | 3 mo. | 128 | | | | | | | | | | | | |
| | 10/30 | 4½ mo. | ... | .. | .. | .. | .. | .. | 11.2 | 5.9 | 66 | B3 O2 | Definite healing of distal end of ulna; dense bones; poor centers of ossification | | |
| Case 5 | 7/25 | 12 days | ... | .. | .. | .. | .. | .. | 11.0 | 5.3 | 58 | ..... | ..... | Fifteenth day | |
| Negro; | 10/17 | 3 mo. | 184 | .. | .. | .. | .. | .. | 11.5 | 6.8 | 78 | ..... | Doubtful rickets of costochondral junctions | ..... | Very rapidly growing infant |
| 1,280 Gm.; | | | | | | | | | | | | | | | |
| 37.7 cm. | 12/15 | 5 mo. | 292 | | | | | | | | | | | | |
| Case 6 | 4/11 | 20 days | ... | .. | .. | .. | .. | .. | 11.5 | 6.8 | 78 | ..... | ..... | Twentieth day; viosterol 100 D | |
| Negro; | | | | | | | | | | | | | | | |
| 1,980 Gm.; | 6/20 | 3 mo. | 85 | .. | .. | .. | .. | + | 10.4 | 6.7 | 70 | A2 O2 | Moderate active rickets with moderate osteoporosis | | |
| 43.9 cm. | | | | | | | | | | | | | | | |
| | 8/15 | 5 mo. | 210 | | | | | | | | | | | | |
| | 10/24 | 7 mo. | ... | .. | .. | .. | .. | .. | 10.9 | 6.4 | 74 | C1 O1 | Summer healing | | |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case 7 | 1/23 | 11 days | ... | .. | .. | .. | .. | .. | 10.8 | 6.5 | 70 | ..... | ..... | Twelfth day | Twin |
| white; | 2/27 | 6 wk. | 43 | .. | .. | .. | .. | .. | 10.2 | 5.1 | 52 | | | | |
| 2,780 Gm. | 4/17 | 3 mo. | 91 | .. | .. | .. | .. | .. | 11.2 | 6.4 | 72 | B2 O1 | Ossification centers ragged, thin | | |
| | 6/ 5 | 5 mo. | 150 | .. | .. | .. | + | .. | 11.6 | 6.8 | 79 | B1 O0 | | | |
| Case 8 | 7/11 | 7 days | ... | .. | .. | .. | .. | .. | 12.2 | 6.1 | 74 | ..... | ..... | Seventh day | |
| white; | 8/22 | 7 wk. | 76 | .. | .. | .. | .. | .. | 11.5 | 7.2 | 83 | A1 O2 | Flares at distal end of ulna | | |
| 1,700 Gm.; 41 cm. | 10/ 3 | 3 mo. | 159 | .. | .. | .. | .. | .. | 11.5 | 6.0 | 69 | | | | |
| | 12/26 | 5 mo. | 241 | .. | + | .. | + | .. | 10.8 | 6.5 | 70 | B1 O2 | Shaft thickened laterally; ulna flared; mild healing rickets | ..... | Rapidly growing infant |
| Case 9 | 2/13 | 10 days | ... | .. | .. | .. | .. | .. | 10.2 | 5.9 | 60 | ..... | ..... | Tenth day | |
| white; | 3/13 | 6 wk. | 67 | .. | .. | .. | .. | .. | 10.4 | 6.2 | 64 | | | | |
| 1,810 Gm.; 42.5 cm. | 5/ 1 | 3 mo. | 150 | .. | .. | .. | .. | .. | 11.6 | 6.2 | 72 | A1 O1 | Very mild osteoporosis; ossification centers present but ragged | ..... | Sudden unexplained death at 4 months |
| Case 10 | 1/30 | 7 days | 41 | .. | .. | .. | .. | .. | 11.2 | 5.2 | 58 | ..... | ..... | Fourteenth day | Twin |
| Negro; 2,240 Gm.; 45 cm. | 4/17 | 3 mo. | 91 | .. | .. | .. | + | .. | 10.4 | 6.0 | 62 | B1 O1 | Ragged ossification centers, both legs | | |
| | 6/20 | 5 mo. | 155 | | | | | | | | | | | | |
| | 8/14 | 7 mo. | ... | .. | .. | .. | .. | .. | 11.2 | 6.1 | 68 | C1 O0 | Healed rickets of very mild degree | | |
| Case 11 | 11/13 | 22 days | ... | .. | .. | .. | .. | .. | 11.2 | 4.8 | 54 | ..... | ..... | Seventh day | |
| white; | 12/ 2 | 6 wk. | 54 | .. | .. | .. | .. | .. | 11.2 | 6.6 | 74 | | | | |
| 2,810 Gm.; | 1/23 | 3 mo. | 100 | .. | .. | .. | .. | .. | 11.2 | 5.7 | 64 | | | | |
| 48 cm. | 3/15 | 5 mo. | 157 | .. | + | .. | + | .. | .... | ... | .. | B1 O1 | Doubtful rickets | | |
| Case 12 | .... | ..... | ... | .. | .. | .. | .. | .. | .... | ... | .. | ..... | ..... | Tenth day | Twin |
| white; | 6/27 | 6 wk. | 37 | .. | .. | .. | .. | .. | 11.5 | 6.5 | 75 | | | | |
| 1,930 Gm.; | 8/ 7 | 3 mo. | 116 | | | | | | | | | | | | |
| 43.3 cm. | 10/ 8 | 5 mo. | 163 | .. | + | | | | | | | | | | |
| | 11/ 7 | 6 mo. | ... | .. | .. | .. | .. | .. | 11.0 | 5.6 | 62 | C1 O1 | Cortex poorly defined, shaft thickened; mild early rickets, now healed | | |
| Case 13 | 6/ 6 | 18 days | ... | .. | .. | .. | .. | .. | 9.6 | 7.6 | 73 | ..... | ..... | Tenth day | Twin |
| white; | 6/27 | 6 wk. | 30 | .. | .. | .. | .. | .. | 9.6 | 6.5 | 62 | | | | |
| 1,960 Gm.; | 8/ 7 | 3 mo. | 95 | | | | | | | | | | | | |
| 43 cm. | 10/ 8 | 5 mo. | 135 | .. | + | .. | + | .. | .... | ... | .. | ..... | Thickening of shaft, cortex poorly defined; mild early rickets, now healed | | |
| | 11/ 7 | 6 mo. | ... | .. | .. | .. | .. | .. | 12.0 | 6.5 | 78 | C1 O1 | | | |

* For the purpose of clarity and brevity we have used the letters A, B, C as follows: A, active progressive rickets without evidence of healing; B, the rachitic process in balance, that is, with evidence of healing in the presence of continued activity, and C, healed rickets without evidence of activity. Osteoporosis is represented by O. The degree of the rachitic involvement and osteoporosis is graded by the numbers 1, slight; 2, moderate; 3, marked, and 4, severe involvement. Negative clinical findings are represented by blank spaces rather than by zeros. Positive clinical findings are represented in the order of severity, on the scale of +, ++, +++ and ++++.

other minerals. He gave the following figures of Fehling for the content of water and mineral ash at various fetal ages: 6 weeks, 97.5 per cent water, 0.001 per cent mineral ash; 6 months, 89 per cent water, 1.94 per cent mineral ash; at term, 71 per cent water, 3.30 per cent mineral ash. Muhl [27] agreed with Michel [28] and Hugounenq [29] that the premature infant lacks the depot of calcium laid down in the last fetal months, but considered that the retention of calcium of the premature infant is on a level with or higher than that of the full-term infant. Hamilton [30] stated that 85 per cent of the calcium supply of the newly born infant is stored during the last two to three months of fetal life. In a later article Hamilton [31] said that the postnatal retention of calcium in normal infants fails for a time to keep pace with the structural growth, so that the calcium concentration in the body as a whole tends to fall throughout the early months, reaching a minimum at the fourth to the fifth month of life. The fact that the normal breast-fed infant excretes about 0.2 Gm. of calcium oxide daily, regardless of the intake, indicates that this amount of calcium oxide is needed for internal metabolism, probably for the neutralization and removal of acid substances. He found also that the retention of calcium of the premature infant is particularly small during the first two to four months. Therefore, in the premature infant, especially in one who is thriving, there is, on account of the rapid rate of growth, an even more active dissipation of an already deficient calcium depot than in the normal infant. An intake of calcium in excess of 0.2 Gm. a day is necessary in the premature infant, since this amount is required for internal metabolism and only a small amount is available for retention in the bones. The retention of phosphorus in normal full-term infants is greater than the retention of calcium and is sufficient to prevent a decrease in the store of phosphorus. The retention of phosphorus in the premature infant apparently parallels that of the full-term infant, and in this respect differs from the retention of calcium.

There is a considerable paucity of data on the values of the serum calcium and inorganic phosphorus of the normal and premature infant

27. Muhl, G.: The Fat Absorption and the Calcium Metabolism of Prematurely Born Infants, Acta paediat. **5**:188 (Oct.) 1925.

28. Michel, C.: Sur la composition organique et minérale du foetus et du nouveau-né, Obstetrique **5**:253 (May) 1900; Sur la composition chimique de l'embryon et du foetus humains aux différentes périodes de la grossesse, Séances et mém. Soc. de biol. **51**:422 (May) 1899.

29. Hugounenq, M. L.: La statique minérale du foetus humain, J. de physiol. et de path. gén. **2**:509 (July) 1900.

30. Hamilton, B.: The Calcium Metabolism of Premature Infants, Am. J. Dis. Child. **20**:316 (Oct.) 1920.

31. Hamilton, B.: The Calcium and Phosphorus Metabolism of Prematurely Born Infants, Acta pædiat. **2**:1 (July) 1922.

at birth and through the early months of life. A brief survey of the more important investigations of calcium values prior to the studies of Bakwin and Bakwin [32] on the new-born infant was given by them in 1932, and is shown in table 3. The figures show a considerable variation: from 10.75 to 12.7 mg. per hundred cubic centimeters.

Bakwin and Bakwin found no correlation between the weight at birth and the serum calcium content in the white new-born infants. They found the average for 14 infants (whose weight at birth was 2,500 Gm. or under) to be 11.08 mg. per hundred cubic centimeters, and believed that this was of interest in relation to the frequency with which rickets and tetany occur in the premature infant.

Alfred Hess,[4] in 1929, said that the normal concentration of inorganic phosphorus in the blood of infants, as determined by the Clark-

TABLE 3.—*The Serum Calcium Values of the New-Born Infant, According to Various Authors (from Bakwin and Bakwin [32])*

| | Number of Estimations | Average Serum Calcium, Mg. per 100 Cc. | Standard Deviation, Mg. per 100 Cc. |
|---|---|---|---|
| Howland and Marriott | 4 | 10.9 | |
| Jones | 68 | 12.3 | |
| Hess and Matzner | 18 | 10.75 | |
| Howland and Kramer | 7 | 10.8 | |
| Bogert and Plass | 23 | 10.98 | 0.73 |
| György | 23 | 11.0 | |
| Nohlen | 19 | 12.70 | 0.45 |
| Abarel and Ornstein | 20 | 10.62 | 1.18 |
| Bakwin and Bakwin | 300 | 11.0 | 0.92 |

Collip method, varied from 6 to 4.75 mg. per hundred cubic centimeters of plasma. The relation of changes in the values for blood calcium and phosphorus to rickets was well summarized by Hess [4] in the following statement:

> . . . the chemical examination of the blood is not an infallible criterion (of rickets) in infants. . . . At times the level of inorganic phosphate is within normal limits, in spite of the fact that undoubted clinical signs of rickets are present. This undoubtedly occurs in premature infants, who, as a rule, have a high concentration of inorganic phosphorus. The calcium concentration remains unchanged or but slightly lowered except where tetany is present, either in manifest or latent form, under which circumstances the normal concentration of about 10 mg. falls to a greater or less degree.

Hess, Weinstock, Rivkin and Gross [33] reiterated Hess' belief that rickets may be associated with a normal concentration of inorganic

32. Bakwin, H., and Bakwin, R. M.: Factors Influencing the Calcium Concentration in the Serum of New-Borns, Am. J. Hyg. **15**:766 (May) 1932.

33. Hess, A.; Weinstock, M.; Rivkin, H., and Gross, J.: The Lack of Relationship Between the Development and Cure of Rickets and the Inorganic Phosphorus Concentration in the Blood, J. Biol. Chem. **87**:37 (May) 1930.

phosphorus in the blood. They thought that although rickets is usually associated with a decrease of the content of inorganic phosphorus, this diminution cannot be regarded as an essential or inherent feature in the pathogenesis of this disorder, and that there is probably a local disturbance at the epiphysis which prevents the anchorage of calcium and phosphorus in the cartilage and bone.

We have studied the values for serum calcium and inorganic phosphorus at birth in full-term and premature infants for comparison with those infants who later received no therapy directed against rickets and with those who received viosterol soon after birth. These findings are shown in table 4. It is apparent that there is no appreciable difference in the values for full-term and premature infants at birth.

The values for serum calcium and inorganic phosphorus have been studied in 2 groups of premature infants, the first of which received no antirachitic therapy, and the second of which received viosterol

TABLE 4.—*The Serum Calcium and Inorganic Phosphorus Values of Full-Term and Premature Infants at Birth*

| | Calcium, Mg. per 100 Cc. | | | Inorganic Phosphorus, Mg. per 100 Cc. | | |
|---|---|---|---|---|---|---|
| | Number of Cases | Mean | Standard* Deviation | Number of Cases | Mean | Standard Deviation |
| Full-term | 79 | 10.9 | ±1.0 | 85 | 6.1 | ±0.9 |
| Premature | 118 | 10.8 | ±0.9 | 126 | 6.2 | ±0.8 |

* The standard deviation ($\sigma$) was calculated from the formula $\sigma = \sqrt{\frac{d_2}{N}}$ in which $d$ represents the deviation of each observation from the mean of all observations and $N$ the number of observations.

throughout the first five months as a prophylaxis against rickets. Figure 1 shows the curve of the serum calcium values in untreated premature infants throughout the first five months of life. Although there seems to be a decline in the serum calcium value from a figure at birth of 10.5 (± 0.8) to 9.9 (± 1.5) and a later rise at 5 months to 10.5 (±1.4) mg. per hundred cubic centimeters, the variations in this curve are not statistically significant.[34] It is to be concluded, therefore, that in a group of premature infants receiving no antirachitic therapy, there is no significant variation in the serum calcium values throughout the first five months. Figure 2 shows the curve of inorganic phosphorus for the same group of untreated premature infants.

34. A difference between two mean values ($M_1$-$M_2$) has been regarded as statistically significant only when at least three times greater than the probable error of the difference, computed according to the formula:

$$PE\ (M_1—M_2) = \sqrt{(PE_{M1})^2 + (PE_{M2})^2}$$

The probable error of the mean has been computed according to the formula:

$$PE_M = \frac{0.6745\sigma}{\sqrt{N}}$$

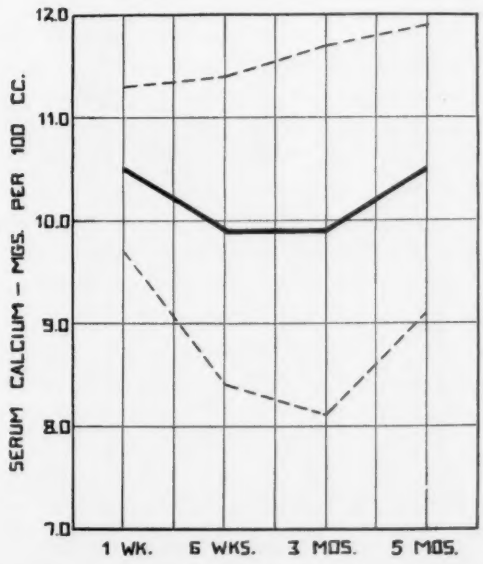


Fig. 1.—The curve of serum calcium in untreated premature infants during the first five months of life. The mean curve is represented by a solid black line, above and below which the two broken lines represent the standard deviation. The distance of one standard deviation from the mean in both directions gives the range within which two thirds of the observations may be expected to fall.

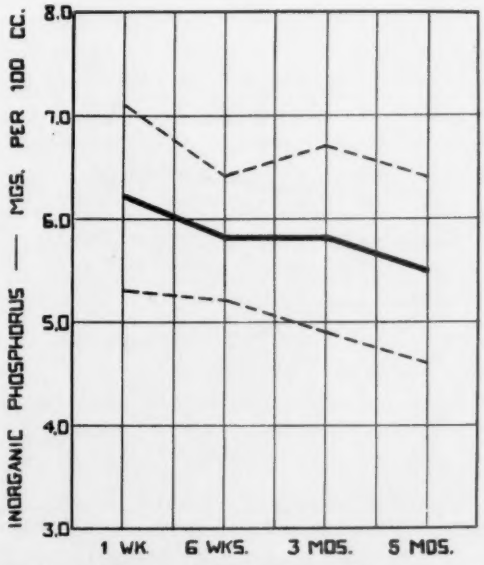


Fig. 2.—The curve of inorganic phosphorus values in untreated premature infants during the first five months.

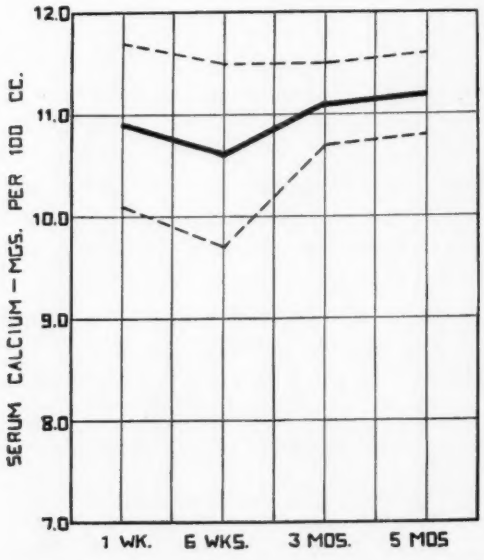


Fig. 3.—The curve of serum calcium in premature infants who received viosterol during the first five months.

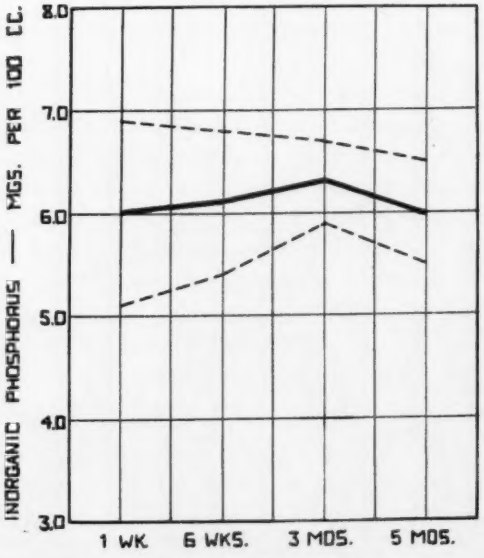


Fig. 4.—The curve of inorganic phosphorus values in premature infants who received viosterol during the first five months.

Although there seems to be a gradual decline from a value at birth of 6.2 (± 0.9) to 5.5 (± 0.9) mg. per hundred cubic centimeters, there is no statistical significance in these variations from the evidence which we have assembled. The inorganic phosphorus in the blood of premature infants receiving no antirachitic therapy apparently does not vary throughout the first five months. Six of 22 of the premature infants who received no antirachitic therapy prior to the development of rickets, by clinical or roentgenographic evidence, were given viosterol or cod liver oil in therapeutic doses from the third to the fifth month after they had shown definite evidence of rachitic involvement. This in turn, however, had no significant influence on the chemical findings of the blood.

Figure 3 shows the curve of the serum calcium in a group of premature infants who received viosterol soon after birth as a prophylaxis against rickets. Although the curve of average calcium values seems to drop less sharply than in the untreated group and to rise to a higher level at the fifth month than in the untreated group, it can be shown that these variations are statistically insignificant. In figure 4 the curve of the inorganic phosphorus values in the same group of premature infants who received viosterol soon after birth parallels the figures of the calcium content, showing no significant variation through the first five months. The results of this study are entirely in agreement with Alfred Hess' statement, already quoted, that the chemical examination of the blood is not an infallible criterion of rickets in infants, since all the infants in the control series showed unmistakable roentgen evidence as well as clinical signs of rickets. In general there is no significant variation of the serum calcium or inorganic phosphorus content through the first five months in the group of untreated premature infants who showed definite rickets of a mild to severe degree clinically and roentgenologically. Eight of these infants (cases 3, 7, 8, 11, 14, 20, 21 and 22, table 1) showed diminution of the serum calcium or inorganic phosphorus content or both below the levels generally associated with active rickets. Three infants (cases 3, 8 and 21) showed latent tetany, 1 at 3 months of age and 2 at 5 months, but these infants did not show greater clinical evidence of rachitic involvement than did the other infants. Tetany developed in case 3 at 5 months of age, with a calcium content of 8.6 mg., an inorganic phosphorus content of 3.4 mg. and a calcium-phosphorus product of 29. There was evidence of marked rachitic involvement both clinically and roentgenologically. The roentgenograms of this infant are shown in figure 4. Tetany developed in case 8 at the age of 3 months, with a calcium content of 7.6 mg., an inorganic phosphorus content of 6.4 mg. and a calcium-phosphorus product of 49. This infant showed only mild clinical and roentgenologic evidence of rickets. Tetany developed in case 21 at the age of 5 months,

with a calcium content of 7.4 mg., an inorganic phosphorus content of 4.6 mg. and a calcium-phosphorus product of 34. There was marked rickets, both clinically and roentgenologically, and the most severe craniotabes seen in any infant in this series.

It is of interest and importance to note also that of the 8 infants only 1 (case 8, table 1) showed a weight increment at 3 months of over 150 per cent, and 3 infants who showed the most marked changes in blood chemistry (cases 14, 20 and 21, table 1) were decidedly under 100 per cent.

In the group of premature infants who received viosterol soon after birth there is, also, no significant variation of the serum calcium or inorganic phosphorus values through the first five months. Therefore no influence of viosterol therapy on these two inorganic elements of the blood has been demonstrated by us.

The calcium-phosphorus product has been generally regarded as helpful in the diagnosis of rickets. Howland and Kramer [35] suggested that a product above 40 should be considered normal; that when the product is between 30 and 40 active rickets is probably present, and that rickets is to be expected when the product is below 30. Hess [4] said that in general this rule holds good, but that it is subject to exceptions, and cited a case of active rickets with a product of 76. In our series of 22 premature infants used as controls who received no antirachitic treatment, 2 showed a calcium-phosphorus product below 30 and one below 40 at a time when marked or severe rickets was demonstrable by roentgenograms. Several showed a product between 40 and 60, but in the majority the product was well above 60. A normal or high calcium-phosphorus product may be considered the rule rather than the exception in the rachitic premature infant, and has been found to be of no diagnostic significance.

### III. ROENTGENOLOGIC CONSIDERATIONS

There is considerable variation of opinion as to the chronology of the sites of the earliest rachitic involvement and as to whether roentgen examination provides earlier evidence of this condition than can be demonstrated clinically. Alfred Hess [19] stated that beading of the ribs often preceded roentgen evidence. Among 149 of his patients showing rachitic changes by roentgenogram, 31 showed changes by roentgenogram and by beading simultaneously, 14 showed changes by roentgenogram before beading and in 104 patients changes were evident by roentgenogram after beading occurred. He used this criterion since he found that the costochondral junctions showed rickets earliest. He found

35. Howland, J., and Kramer, B.: Factors Concerned in the Calcification of Bone, Tr. Am. Pediat. Soc. **34**:204 (May) 1922.

that the wrist was involved next. No other joints showed involvement when the wrist joints were normal. Hess also stated that the joints of the wrists may be enlarged and may give negative roentgenologic evidence. Eliot,[2] on the other hand, stated that the early clinical diagnosis of rickets is much more difficult than early roentgen diagnosis and that one is easily deceived by too much or too little fat. Wimberger [36] quoted Pommer's [37] statement that an increased deposition of uncalcified bone takes place at sites of mechanical strain, in bones growing most rapidly. These are, in order, the costochondral junctions, the distal ends of the femur and ulna, the proximal ends of the humerus and both ends of the fibula. Wimberger stated further that the roentgenogram may give more trustworthy information than even a histologic examination. Weech and Smith [38] considered the chronology of development to be as follows: the costochondral junctions, the proximal ends of the tibia and the humerus and the distal ends of the femur and the radius.

The question of what constitute the earliest roentgen signs of rickets has also been the subject of much controversy. Wimberger [36] used the following criteria: marginal ossification and cupping, coarsening and thinning of the trabeculae (associated with moderate rickets) and osteoporosis, which he interpreted as being a later sign of rickets. The long bones resemble hollow cylinders with the small amount of available calcium deposited at the periphery, resulting in marginal ossification and cupping. The marginal ossification is seen most prominently in the proximal third of the radius and in the laterodorsal portion of the distal half of the shaft of the humerus. Weech and Smith, in correlating the roentgenogram and pathologic observations emphasized, as did Pommer,[37] the evidence of rickets in areas in which growth is fastest. They also outlined other evidence of the active stage of rickets. 1. Rarefaction is one of the most constant findings, often overlooked in the early stages. 2. The sharp termination of the shaft disappears, and the shaft fades into the cartilage in gradually lessening shadows, so that it terminates in a fringe 1 mm. or more in width. 3. There is cupping and lipping of the diaphysis. 4. The cortex loses its compact structure and assumes a more loosely woven pattern. 5. The periosteum is raised from the cortex and is thickened, more frequently on the concave side of the long axis of the bone, but this is evidence which may be present

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36. Wimberger, H.: A Study of Developing, Florid and Healing Rickets as Demonstrated by X-Ray Photography, Medical Research Council, Spec. Rep. Ser. no. 77, London, His Majesty's Stationery Office, 1923, p. 95.

37. Pommer, G.: Untersuchungen über Osteomalacie und Rachitis, Leipzig, F. C. W. Vogel, 1885; cited by Wimberger.[36]

38. Weech, A. A., and Smith, M. S.: The Anatomic Basis for Interpretation of Roentgenograms in Rickets, Am. J. Dis. Child. **26**:117 (Aug.) 1923.

only after healing has taken place. 6. The epiphyseal centers of ossification lose their normal, sharp outline and fade into the cartilage. 7. A transverse line appears in the shaft. Hess outlined his criteria as follows: (1) a general poverty of calcium; (2) irregular cupping of the metaphysis, with fraying; (3) a wide cartilaginous zone between the epiphyseal center and the diaphysis, and (4) periosteal proliferation. Eliot [2] stated that the earliest roentgenologic changes in rickets appear in the distal end of the shaft of the ulna. These constitute at first a slight prolongation of the cortex of the bone, creeping around the cartilage at its periphery. This she interpreted as the first evidence of fraying. Later there is slight cupping of the distal end of the bone, and the end of the shaft is widened with sharp instead of round corners, following which the line of demarcation between the cartilage and the shaft loses its clear outline and may show irregularities.

In a personal communication to the authors, Eliot [39] expressed the belief that a roentgenogram of a premature infant might show important early rachitic changes which had not been apparent in roentgenograms of the full-term infant which she had observed. Eliot [2] also said that by serial films it is possible to trace back the development of rickets from a well defined stage at the age of 6 or 7 months to the earliest changes at 1, 2 or 3 months. We have repeatedly demonstrated by serial roentgenograms this ability to trace back undeniable rachitic changes at the age of 5 or 6 months to their beginning in the early weeks of life.[40] By the use of this method a study of our serial films has emphasized the following changes as of greatest importance in the early diagnosis of rickets in the premature by means of roentgenography: a greater degree of osteoporosis, an earlier and more marked involvement of the periosteum and a greater deposition of uncalcified bone, which in the roentgenogram gives a frayed or chewed out, ragged appearance. These findings have been described and emphasized by various investigators, but they have been so consistently present in our series of untreated premature infants who showed rickets that we believe they are of prime importance as early diagnostic signs.

There has been no question of the gradual development of the classic evidences of rickets at the generally accepted sites at the distal end of

39. Eliot, M. M.: Personal communication to the authors.

40. Various observers have emphasized the importance of uniformity of technic in evaluating serial roentgenograms from the standpoint of progression of the rachitic lesions and reading back from definite, marked involvement to the earlier, more questionable changes in the bone. This is especially true of the duration of the exposure and the quality of tube used. All are agreed that a short exposure with soft rays serves best to bring into sharp outline the faint shadows of rachitic bone. All roentgenograms in this study have been taken according to the following technic: distance, 40 inches (101.6 cm.); time of exposure, ¼ second; milliamperes, 80; kilovolts, 46.

the ulna and radius. Of particular significance was the early and marked deposition of uncalcified bone at the proximal medial surface of the shaft of the ulna, a sign which, we believe, has been hitherto undescribed. Figure 5, upper row, shows the rapid progress of the development of the rachitic process at the distal ends of the ulna and radius and at the

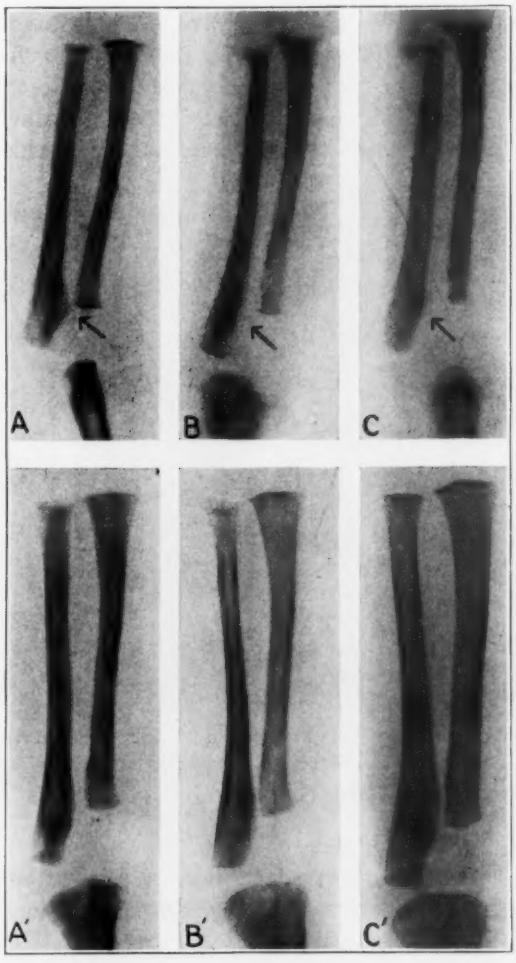


Fig. 5 (case 22).—Upper row: developing rickets in the ulna and radius of a premature infant at (*A*) six weeks, (*B*) 3 months and (*C*) 5 months. Lower row: ulna and radius of normal full-term infant at (*A'*) 6 weeks, (*B'*) 3 months and (*C'*) 5 months.

distal end of the humerus, together with a severe degree of osteoporosis, at the age of 6 weeks, 3 months and 5 months. Bones of the normal full-term infant at corresponding ages are shown in the lower row.

Films in the rachitic series taken at 6 weeks of age show no evidence of involvement at the distal ends of the ulna and radius. Reading back, however, from later films which show florid rickets, it is evident that the films taken at 6 weeks of age show a beginning fraying and rarefaction of the radial surface of the proximal end of the shaft of the ulna. There is also a periosteal proliferation of the distal end of the humerus. These changes, seen earlier, are progressive in later films, accompanying the obvious pathologic process at the distal ends of the ulna and radius. This early involvement of the proximal ulna with its subsequent progression is shown also in figure 6. In the last of the films, taken at 6 months of age, after three weeks of viosterol therapy, there is evidence of begin-

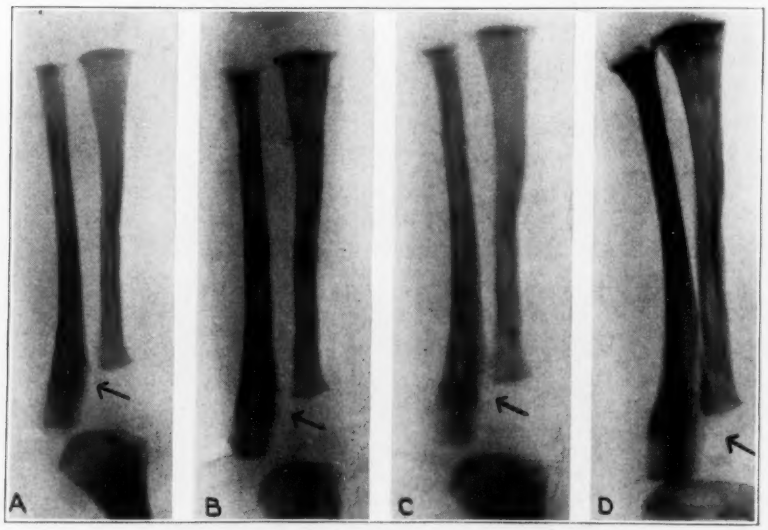


Fig. 6 (case 3).—Progressive involvement of the proximal radial surface of the shaft of the ulna in a rachitic premature infant, with healing at 6 months after three weeks of viosterol therapy: *A*, 6 weeks; *B*, 3 months; *C*, 5 months; *D*, 6 months.

ning healing, with an increased deposition of calcium at the proximal end of the shaft of the ulna and a filling in of the previously frayed out area on the radial surface. Figure 7 shows the progress of the involvement of the proximal end of the ulna together with marked periosteal proliferation of the shaft of both ulna and radius. In this infant, however, the periosteal proliferation is most marked in the femur. There are also thickening of the cortex, osteoporosis of the distal ends of the tibia and cupping and flaring of the metaphyses of all of these bones. We have no histologic proof to offer in support of our claim that this change in the proximal end of the ulna is rachitic; but its occurrence in association with established evidences of rickets in other parts of the

body, its absence in normal or in only mildly rachitic infants and, particularly, its characteristic healing under the influence of an adequate administration of viosterol, running parallel as it does with healing elsewhere, leave little ground for question. Detailed descriptions of

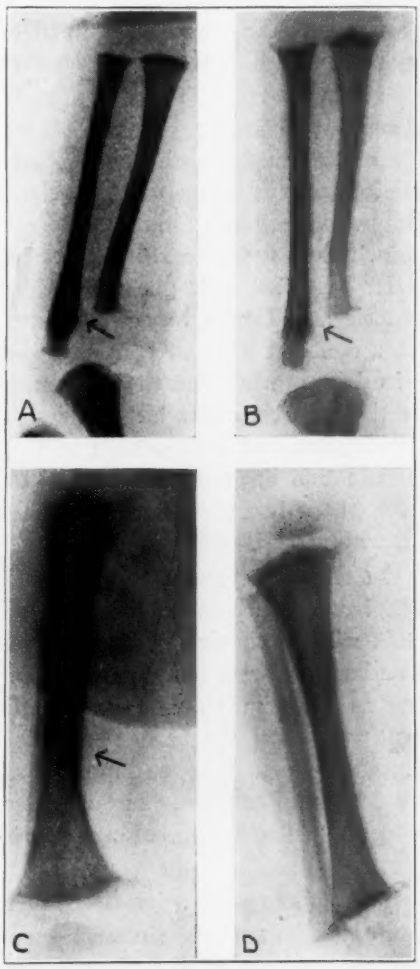


Fig. 7 (case 7).—Fraying and rarefaction of the proximal ends of the ulnar shaft; marked periosteal proliferation, particularly of the femur, in a rachitic premature infant; *A*, 6 weeks; *B*, *C* and *D*, 5 months.

the degree and stage of rachitic involvement of the bones as shown by the roentgenograms are given in tables 1 and 2.

A study of untreated cases from a roentgenologic standpoint (table 1) makes evident the following facts: A great majority of the infants show definite roentgenographic evidence of rachitic involvement at the

age of 6 weeks, before there is any manifestation of rickets by clinical or chemical examination. The fraying of the proximal end of the ulna occurs with sufficient regularity to make this an important early sign. As has been stated, the fraying may be only suggestive at 6 weeks, and can be corroborated only by later examination, but knowledge of this tendency of early involvement of the proximal end of the ulna should direct close scrutiny to this area in the roentgenogram when other evidence of rickets is lacking.

The early and rapidly advancing osteoporosis of the long bones, which has regularly accompanied the development of other changes in bone, makes us believe that this is one of the early and most constant roentgenologic findings. Weech and Smith [38] referred to this condition as "rarefaction," which they stated was often overlooked in the early stages, and Alfred Hess [4] called it "a general calcium poverty." This tendency to osteoporosis would seem very probably to be related in the premature infant to a deficient store of calcium at birth and an insufficient absorption of calcium throughout the early months, together with a rearrangement of the bone calcium which results in a withdrawal of calcium from the trabeculae and a deposition in the marginal cortex. Osteoporosis has been found in general to parallel the development of other rachitic changes in the bones, so that marked active rickets ($A_3$) is usually associated with marked osteoporosis ($O_3$).

Coarsening of the trabeculae and thickening of the cortex from marginal ossification have been common findings. Wimberger [36] and Eliot [2] associated this with mechanical strain. Periosteal proliferation has been an early finding, and also an especially prominent one. This manifests itself first as a general thinning and haziness of the lateral margins of the shaft and often can be demonstrated only by reading back from later films, in which the proliferated periosteum is sharply outlined by a heavy deposit of calcium. In our experience this process often accompanies continued activity, before antirachitic therapy has been instituted.

With these roentgen signs in mind reference to table 2, which records the findings in the infants who received viosterol soon after birth, shows that in all but 1 infant evidence of definite mild rickets was demonstrated by roentgenogram. The importance of early and frequent films of the long bones was not apparent during the observation of our treated cases, and many of these infants had but one or two roentgen examinations from the third to the sixth month. Comparison of these, however, with films in untreated cases left no question in our minds of the presence of previous mild rickets which was healing or had healed. These infants coincidentally were almost entirely free from clinical signs or chemical evidence of rickets, and had it not been for the roentgenograms,

we should have considered them adequately protected by viosterol in the dosage used. This study substantiates the ideas of other investigators, principally Alfred Hess,[4] that viosterol 250 D in a maximal dosage of 20 drops a day is not adequate for the prophylaxis of rickets in the premature infant.

To summarize: As rickets progresses in untreated infants the involvement of the long bones as shown by roentgenogram appears at a considerably earlier time and is definitely more advanced at successive age periods than can be demonstrated by clinical or chemical criteria. The roentgenogram must be regarded, therefore, as the criterion of prime importance in the early diagnosis of rickets.

TABLE 5.—*Serum Calcium and Phosphorus Values in Relation to Craniotabes, Osteoporosis and the Calcium-Phosphorus Product in Premature Infants with Marked or Severe Rickets*

| Case | Serum Calcium, Mg. per 100 Cc. | Serum Phosphorus, Mg. per 100 Cc. | Severity of Craniotabes | Degree and Stage of Rickets and Osteoporosis | Calcium, Phosphorus Product |
|---|---|---|---|---|---|
| 14 | 6.2 | 4.2 | 0 | A4 O4 | 26 |
| 11 | 7.2 | 6.3 | + | A3 O4 | 45 |
| 21 | 7.4 | 4.6 | ++++ | A3 O3 | 34 |
| 7 | 7.8 | 5.1 | ++ | B4 O4 | 40 |
| 13 | 8.0 | 5.7 | 0 | A3 O3 | 46 |
| 3 | 8.6 | 3.4 | ++ | A3 O3 | 29 |
| 20 | 9.0 | 4.6 | 0 | A4 O4 | 41 |
| 22 | 9.4 | 4.4 | +++ | A4 O4 | 41 |
| 6 | 10.8 | 6.2 | 0 | C4 O3 | 67 |
| 19 | 11.8 | 5.8 | ++ | A3 O3 | 68 |

IV. SERUM CALCIUM VALUES, OSTEOPOROSIS AND CRANIOTABES

The possible relation of craniotabes to osteoporosis and a lowered serum calcium level in those untreated infants in whom marked to severe rickets was shown by roentgenogram is shown in table 5. Of the 10 infants who showed marked to severe rickets by roentgenogram, 4 showed no craniotabes, 1 showed 1 plus, 3 showed 2 plus, 1 showed 3 plus and 1 showed 4 plus. The serum calcium content, which was determined coincidentally with the roentgen and clinical observation, was below 10 mg. per hundred cubic centimeters, except in 2 cases. One of these patients (case 6) was an infant, born in the summer, and the only roentgenogram was taken in late October when he was 4½ months of age. This showed severe rickets with marked healing ($C_4 O_3$) and a serum calcium concentration of 10.8 mg. and a calcium-phosphorus product of 67. The other (case 19) was an infant born in the winter and the roentgenogram showed marked active rickets ($A_3 O_3$) with a serum calcium concentration of 11.8 mg. and a calcium-phosphorus product of 68.

There would seem to be some connection, therefore, between a lowered serum calcium level and marked osteoporosis, but the nature of this relationship and the etiologic factors concerned are not, so far as we are aware, understood. No comparable relation of the severity of craniotabes to either progressive osteoporosis or a decrease in serum calcium can, however, be assumed.

SUMMARY

1. A comparison of clinical, chemical and roentgenologic evidence of the development of rickets has been made in a group of premature infants who received no antirachitic therapy from birth to the age of 5 months.

2. The diagnosis of rickets has been possible at a considerably earlier age by the roentgenogram than by clinical evidence in the majority of cases.

3. Rarefaction and fraying of the radial surface of the proximal end of the shaft of the ulna, a finding hitherto undescribed, has been an early and significant sign of rachitic involvement in the premature infant. This has often been apparent at the age of 6 weeks, before the appearance of signs in other portions of the bones. Marked osteoporosis, periosteal proliferation and thickening of the cortex have also been found to be characteristic of early rickets.

4. No significant variation of serum calcium or inorganic phosphorus from birth to 5 months of age has been observed, even in the presence of severe clinical and roentgenologic rickets.

5. It has been shown that viosterol 250 D in a maximal dosage of 20 drops a day has been inadequate for the complete protection of the premature infant.

6. No influence of the rapidity of growth on the severity or the rate of development of the rickets has been observed.

7. Low serum calcium values, when found, tended to occur in infants in whom osteoporosis was shown by roentgenogram; but no close correlation could be established between the serum calcium level, the degree of osteoporosis and the severity of craniotabes.

# LIPOID CELL PNEUMONIA

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For some years proliferative pneumonia following the aspiration of fatty material into the lung has been recognized as a pathologic entity, but never as a clinical one. It seems wise, therefore, to report the experiences of my associates and myself with lipoid cell pneumonia, because of its fairly consistent clinical picture in well marked cases, its frequency and the possibility of its prevention.

In 1885, and again two years later, Rosenberg [1] reported the successful treatment of infections of the lungs by the intratracheal injection of medicated olive oil. At this time Sehrwald [2] was using percutaneous tracheal puncture and injection to accomplish the same purpose, but neither of these workers mentioned pneumonia as a complication of their therapeutic procedures. The enthusiasm for intratracheal administration of antiseptics waned until Campbell [3] revived the method in 1895. Although Campbell introduced as much as 20 cc. of the oil at one time and repeated this dose frequently, he likewise failed to mention any reaction in the lungs. Careful studies of the pathologic process were not made in his fatal cases.

Little further progress was made toward an understanding of the effects on the lungs of the introduction of oil until attempts were made to introduce opaque substances for purposes of pneumonoroentgenography. Waters, Bayne-Jones and Rowntree [4] made a significant advance toward this end in 1917 when they found that in the 25 per cent of their animals dying after the injection of 10 per cent iodoform in

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From the Harriet Lane Home of the Johns Hopkins Hospital and the Department of Pediatrics, Johns Hopkins University.

1. Rosenberg, A.: Zur Behandlung der Kehlkopf-und Lungentuberculose, Berl. klin. Wchnschr. **24**:466, 1887; Das Menthol, ein Ersatz des Cocain zur Erzeugung localer Anasthesie in Nase und Pharynx, ibid. **22**:449, 1885.

2. Sehrwald, E.: Ueber die percutane Injection von Flüssigkeit in die Trachea, deren Verbreitung in die Lunge und Wirkung auf Lunge und Gesamtorganismus, Deutsches Arch. f. klin. Med. **39**:162, 1886.

3. Campbell, Colin: The Treatment of Respiratory Infections by Means of Large Medicinal Injections Through the Larynx, Med.-Chir. Tr., London **78**:38, 1894.

4. Waters, C. A.; Bayne-Jones, S., and Rowntree, L. C.: Roentgenography of the Lungs, Arch. Int. Med. **19**:543 (April) 1917.

olive oil a proliferative bronchopneumonia was present. "In all cases exudate was found to be undergoing organization while the alveolar and bronchial epithelium was considerably hypertrophied."

The next contribution of importance came in 1920 when Guieysse-Pellissier [5] injected olive oil into the lungs of rabbits and found that it was absorbed by large mononuclear cells which he believed to be proliferative alveolar epithelium. When Corper and Freed [6] performed similar experiments on guinea-pigs two years later, they discovered that olive oil and liquid petrolatum produce a chronic proliferative bronchopneumonia. When chaulmoogra oil or its esters were mixed with the other oils, a rapid and violent pulmonary inflammation ensued which often led to hemorrhage and gangrene.

In 1926, Iglauer [7] pointed out that the combination of iodine and oil used in making roentgenograms remained in the lungs for a long time after injection and was eliminated by absorption as well as by expectoration. In some instances he found oil in the alveoli five months after its administration. Brown [8] (1928) added to the knowledge when he described the production of an infiltration of mononuclear cells around healthy alveoli following the injection of iodized oil. He considered these phagocytes to be endothelial cells. The controversy over the origin and nature of mononuclear phagocytes in the lungs has not reached a satisfactory conclusion. Excellent reviews on this subject are those of Permar [9] and Foot.[10]

Lipoid cell pneumonia in man was not described until 1925 when Laughlen [11] reported three instances occurring in children following the nasopharyngeal administration of liquid petrolatum, and one instance in an adult with pharyngeal paralysis. Laughlen called attention to the dense character of the consolidation caused by the crowding of the alveoli with large mononuclear phagocytes packed with droplets of the emulsified oil. He also brought out the point both from cases coming to autopsy and from experiments in animals that infection usually accom-

5. Guieysse-Pellissier, A.: Recherches sur l'absorption de l'huile dans le poumon, Compt. rend. Soc. de biol. **83**:809, 1920.

6. Corper, H. J., and Freed, Harold: The Intratracheal Injection of Oils for Diagnostic Therapeutic Purposes, J. A. M. A. **79**:1739 (Nov. 18) 1922.

7. Iglauer, S.: Injected Iodized Oil in Roentgen Ray Diagnosis of Laryngeal, Tracheal and Bronchopulmonary Conditions, J. A. M. A. **86**:1879 (June 19) 1926.

8. Brown, A. Lincoln: Fate of Iodized Oil (Lipiodol) in the Lungs, Surg., Gynec. & Obst. **46**:597 (May) 1928.

9. Permar, H. H.: Mononuclear Phagocytes in Experimental Pneumonia, J. M. Research **44**:27 (Sept.) 1923.

10. Foot, N. C.: Endothelial Cell in Experimental Tuberculosis, J. Exper. Med. **32**:513 (Nov.) 1920.

11. Laughlen, G. F.: Pneumonia Following the Nasopharyngeal Injections of Oil, Am. J. Path. **1**:407 (July) 1925.

panies pneumonia caused by fat. Oily substances placed in the nose or pharynx may find their way to the lungs through the trachea and may carry infection with them.

Laughlen's work seemed to excite new interest in this field, and stimulated by it, Thomas and Jewett [12] (1926) reported a case of pneumonia following the aspiration of a large quantity of cream. The following year a significant contribution was made by Pinkerton [13] when he reported six cases of inflammation of the lung caused by the aspiration of fats. The cases varied in the type of oil aspirated as well as in the length of time the oil had been in the lung. This knowledge enabled him to give a clear account of the pathologic sequences following the arrival of oil in the alveoli. In a few hours mononuclear phagocytes appeared in the alveoli, engulfing the smaller droplets of oil as the fat became emulsified. Within a few days the portions of the lung containing the oil became densely consolidated with large numbers of these wandering mononuclear cells, many of which had coalesced to form giant cells. A few of the cells slowly found their way out of the alveoli to the lymphatics and finally to the bronchial lymph nodes. Frequently the lymphatics were blocked with masses of free fat and fat-holding cells. The final stage in the pathologic process in his cases was fibrosis of the lung occurring first as a mere thickening and infiltration of the interalveolar septums, and later going on to the formation of fibrous nodules, 3 cm. in diameter, around the larger collections of lipoid material. Some of these nodules were described as being tubercle-like. An interesting account was given by Simonds [14] of the development of tubercle-like structures in the lungs of rabbits following the intravenous injection of emulsified suprarenal gland. He believed that it is the high content of fat that causes this particular form of foreign body reaction.

Pinkerton noticed, as Laughlen did, the frequent association of infection in the lung with lipoid cell pneumonia. In two of his cases, however, there was little or no fever, which he gave as a point of possible clinical significance. Roentgenograms in his cases did not show anything characteristic. Pinkerton suggested examination of the sputum for oil-laden phagocytes as a means of diagnosis.

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12. Thomas, W. S., and Jewett, C. H.: Pneumonia Following the Aspiration of Fats from the Esophagus Dilated as a Result of Cardiospasm, Clifton M. Bull. **12**:130, 1926.

13. Pinkerton, Henry: Oils and Fats: Their Entrance into and Fate in Lungs of Infants and Children: Clinical and Pathologic Report, Am. J. Dis. Child. **33**: 259 (Feb.) 1927.

14. Simonds, J. P.: Organization of Experimental Adrenal Cell Emboli in Lungs, Am. J. Path. **3**:13 (Jan.) 1927.

The work of Pinkerton [15] in 1928 did a great deal to clarify the pathogenesis of the changes in the lungs following the aspiration of different fats. He concluded that the severity of the immediate reaction in the lung was largely due to the amount of fatty acid present or produced from the oil aspirated. The mild vegetable oils, such as poppy seed, olive and sesame oil, caused the least reaction, while cod liver oil, lard and other animal fats caused a sudden and often violent reaction in the lungs, with hemorrhage and necrosis. Aspiration of liquid petrolatum was followed by the production of proliferative pneumonia. Large mononuclear phagocytes, engulfing the small particles of fat, filled the alveoli. Giant cells were common, and there was much fibrosis of the lung. This kind of reaction seemed to correspond most closely to that observed in the cases which Pinkerton previously described.[13]

Case 1 is noteworthy because it indicates the existence of lipoid cell pneumonia as a clinical entity.

## REPORT OF CASES

CASE 1.—A. P., a white boy, 4 months of age, was admitted to Harriet Lane Home on Nov. 8, 1929, with the history of failure to gain weight and a cough of two months' duration. An agent, who was a frequent visitor to the house, and who was known to have played with the baby, had active tuberculosis. Active tuberculosis developed in the father soon after the child's admission to the hospital. The Wassermann reaction in both parents was positive. A sister, 2½ years of age, and a brother, 16 months of age, were well. The mother seemed well.

The birth of the patient was without unusual incident, and the first two months of life were uneventful. At the beginning of the third month a cold developed. This was soon followed by vomiting and diarrhea, which lasted several weeks. The milk formula was changed many times in an attempt to stop the gastro-intestinal disturbance. Nose drops of liquid petrolatum were given for the infection of the upper respiratory tract. These were administered several times a day for three or four weeks. Failure to gain weight and the cough caused the child to be brought to the hospital.

The patient presented the picture of a chronically ill child, although in no particular distress. Flabby muscles and redundant skin suggested a recent loss of weight. There was moderate cyanosis, and slight but definite clubbing of the fingers was noted. Rapid, shallow respirations were punctuated every few minutes by a rasping unproductive cough. The pharynx was inflamed. Scattered moist râles were found in the interscapular region and below the right clavicle, and in these situations the percussion note was dulled and breath sounds were diminished. The spleen was palpable. Otherwise the physical examination did not reveal any abnormality. The leukocyte count was 13,000 and the polymorphonuclears were 78 per cent.

With physical signs of a chronic pulmonary disease and a history of contact, the first thought was of tuberculosis. The roentgenogram (fig. 1) of the lungs showed a bilateral consolidation extending out from the hilus, more marked on the

15. Pinkerton, Henry: Reaction to Oils and Fats in Lung, Arch. Path. **5**:380 (March) 1928.

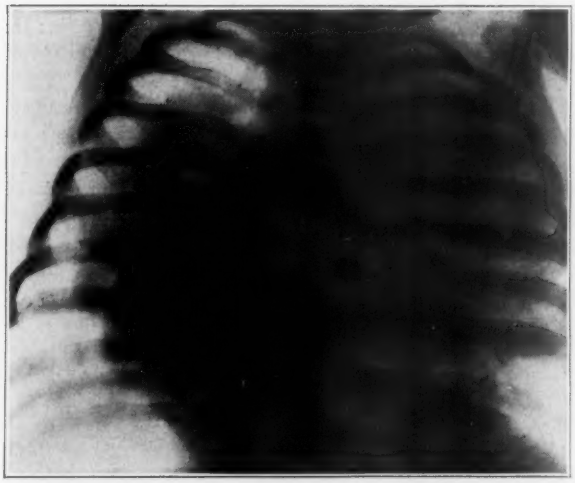

Fig. 1.—Roentgenogram of A. P., Nov. 23, 1929, aged 4 months, showing extensive lipoid cell pneumonia involving most of the right lung and much of the central part of the left lung.

Fig. 2.—Roentgenogram of A. P., July 7, 1930, showing a slight clearing of the consolidation. The chest gives the appearance of having grown away from the area of chronic pneumonia.

right. There was much more evidence of pulmonary involvement in the roentgenograms than there was on physical examination, a discrepancy which fitted in with the idea of tuberculosis. But the reaction to the intracutaneous tuberculin test was repeatedly negative to 1 and even to 5 mg. of tuberculin; human, bovine and avian tuberculin were used. Numerous stomach washings were examined microscopically and found negative for the tubercle bacillus. Two inoculations of guinea-pigs, one from a lung puncture, also gave negative results.

These tests, as well as the afebrile course, made tuberculosis seem unlikely. There was no evidence of fungous infection by culture or microscopic examination of the sputum, and spirochetes could not be demonstrated in dark field illumination. A negative Wassermann reaction and the normal appearance of the long bones of the extremities and ribs in the roentgenogram seemed to rule out syphilis as a cause of the pulmonary changes. The gradual clearing of the lesion was unlike that of a tumor or congenital malformation (fig. 2).

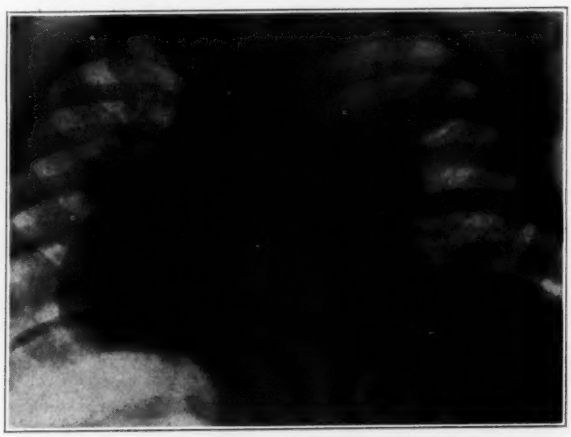

Fig. 3.—Roentgenogram of A. P., Nov. 10, 1930, showing further clearing of the pneumonia fourteen months after the onset.

During the ten months the child was in the hospital the improvement was slow but steady. The temperature was normal except during a few slight respiratory infections. The urine remained normal, and there were no changes in the blood picture. Although growing less in frequency and intensity, the cough persisted throughout his stay of ten months in the hospital. At the age of 14 months the child was discharged, slightly undersized and weighing 6 Kg.; he was able to sit alone, but not to stand or talk.

After two months of improvement he contracted acute otitis media, which caused his readmission to the hospital. The infection, which was streptococcic, spread to the mastoid cells and then to the meninges, causing death. The findings on physical examination of the lungs remained unchanged except for a diminution in the amount of percussion dulness and a corresponding decrease in the size of the roentgen shadow (fig. 3). The chest seemed to have grown away from the central consolidation. During the last day of life signs of congestion were present at the bases of both lungs.

The staff of the Harriet Lane Home was much in doubt as to the nature of the process in the lung. The prevailing opinion favored atypical tuberculosis, even in

the face of negative laboratory evidence. The opinion of the minority was inclined toward chronic interstitial pneumonia.

At autopsy, as was expected, a purulent meningitis of mastoid origin was found. When the lungs were examined in the gross, they were found to be heavy, with no sign of pleurisy. On section (fig. 4) an extensive consolidation was seen, involving the central and posterior portion of both lungs. The air-containing tissue at the apex, the base and the outer surface seemed emphysematous. The consolidated area itself was firm to touch and mottled in appearance, some areas being yellow, others gray. The characteristic structure of the alveoli was lost, and in many places bands of fibrous tissue could be seen radiating from the bronchi through these areas. Many of the yellowish nodules looked and felt like tubercles, but extensive search did not reveal any acid-fast bacilli. The mediastinal lymph nodes were small, soft and grayish red; they contained no tubercles. The microscopic

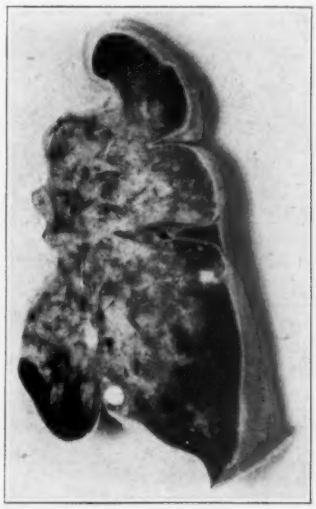

Fig. 4.—Section of right lung of A. P., showing central consolidation, a mottled appearance and extensive scarring of the lung.

sections made the condition clear when the alveoli were found loaded with large, fat-containing mononuclear phagocytes. There was much scarring of the lung, and an increase in thickness of the interalveolar septums was seen. The peribronchial lymph channels and bronchial lymph nodes also contained fat. The nodules previously mentioned were identical with tubercles in structure except that at the center were several globules of oil instead of caseous material and tubercle bacilli. Analysis of the fat in the lungs showed it to be liquid petrolatum.

Case 2.—Shortly after the first patient died a second child was admitted to the hospital with the history of chronic cough and failure to gain weight. J. P., a white girl, 4 months of age, was the only child of normal parents. Two grandparents were suffering from tuberculosis and had some contact with the child. The patient was born prematurely, weighing 5 pounds (2,268 Gm.), and except for jaundice lasting for three weeks was quite well until the end of the first month. About this time feeding became difficult, for the patient vomited frequently. A slight

Fig. 5.—Roentgenogram of J. P., Nov. 5, 1930, showing widespread consolidation, more marked on the right side, leaving the periphery clear.

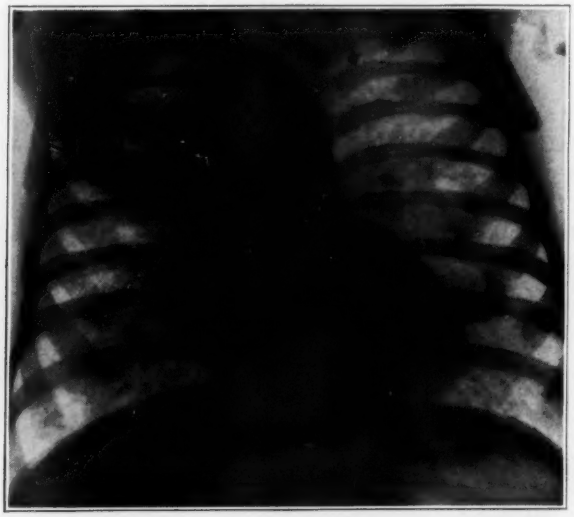

Fig. 6.—Roentgenogram of J. P., Dec. 11, 1930, showing little change in appearance from figure 5.

febrile illness ensued, and the vomiting was intensified. A persistent cough set in and lasted until admission. The history revealed that until the patient's admission at 4 months of age, liquid petrolatum had been given daily by mouth for the relief of constipation.

On admission to the hospital on Nov. 8, 1930, the patient was underdeveloped and malnourished. The temperature was normal, but respirations were rapid and shallow. Percussion revealed impaired resonance over the upper half of both lungs posteriorly, with diminished breath sounds and moist râles in the same area. The liver, spleen and left kidney were enlarged. The right kidney was not felt. A leukocytosis of 18,000, with an increase in mononuclear cells was present, and the urine consistently contained albumin and pus and occasionally casts.

At first the condition was thought to be pulmonary tuberculosis. But the negative reaction to the tuberculin test (5 mg.) and repeated negative stomach washings made it apparent that the condition in the lungs was due to some other cause. The roentgenogram (fig. 5) showed an extensive bilateral infiltration more widespread on the right side and more marked posteriorly. This was very like the appearance in the previous case, leading to the conclusion that lipoid cell pneumonia was the cause of the pulmonary changes. The renal infection progressed rapidly, and the child died five weeks after admission. The condition of the lungs remained the same during the entire stay in the hospital (fig. 6) until pneumonia developed shortly before death. The cough persisted, and cyanosis was occasionally observed.

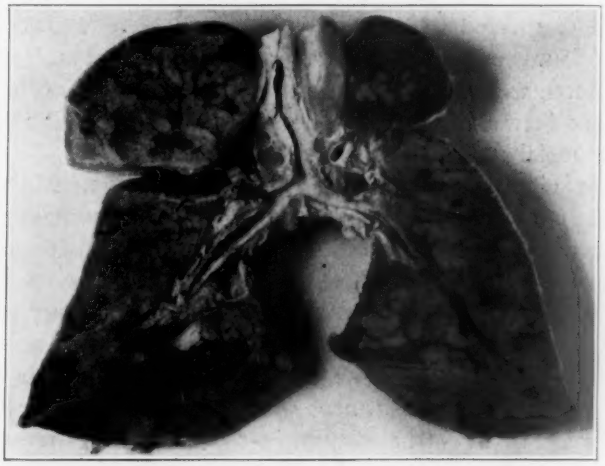

Fig. 7.—Section of both lungs of J. P., showing extensive consolidation, a mottled appearance and comparative freedom from involvement of the apex and base.

At autopsy the surfaces of both lungs were discolored a bluish red, but there was no sign of pleurisy. The anterior edges of the lungs not only contained air but were emphysematous. The posterior portion of both lungs was quite firm. On section (fig. 7) the consolidated area was seen to occupy the central and posterior parts of both lungs. It was yellowish gray, with a few red areas. The normal

markings of the lungs could not be recognized. The fluid on the cut surface showed an oily layer. The bronchi and bronchial lymph nodes showed nothing abnormal.

Microscopic examination showed a fresh lobular pneumonia in certain areas. In others there was nothing but the peculiar changes of lipoid cell pneumonia, with thickened alveolar walls containing many large mononuclear fat-containing phagocytes. There was much scarring in the interalveolar septums. Often there were seen tubercle-like nodules with droplets of fat or small caseous masses in the center surrounded by giant cells, epithelioid cells and fibrous tissue. No tubercle bacilli could be found.

After our attention was called to the pneumonia caused by aspiration of lipoid substances we were able to recognize the condition during life in two additional cases.

During the last ten years twenty-five cases of lipoid cell pneumonia have been discovered in the Harriet Lane Home. In three of these the diagnosis was established clinically; in the others, at autopsy. Twelve of the children were under 6 months of age, six between 6 months and 2 years, six between 2 and 5 years and the oldest, 7. There was no significant racial or sex difference in incidence.

Various oils were responsible for the condition. Milk fat was perhaps the most frequent kind found. The children in these cases were weak or comatose and were fed by gavage, or vomited frequently, and the regurgitation of the milk was undoubtedly the cause of the aspiration. Cod liver oil was present in the lungs in a number of infants, and in almost all there was the story of cough, vomiting or struggling against the administration of the oil. In four of the cases in which the amount of pulmonary involvement was the greatest, a clear history of the instillation of liquid petrolatum in the nose, or its ingestion, was obtained. The oil was identified in the lung in two instances. As has been proved experimentally, a bland oil placed in the nasopharynx can find its way to the lung [11] without inducing symptoms of irritation, such as cough.

## COMMENT

Since, in the present series of cases, this type of pneumonia was nearly always accompanied by some other and more severe illness, evalution of symptoms is difficult. Rapid respiration without dyspnea and a persistent hacking cough stand out as the two most frequent complaints. Failure to gain weight was noted in some of the more chronic cases. Uncomplicated lipoid cell pneumonia produces no fever. In many of the less severe instances no symptoms referable to the lungs were noted. The onset is usually insidious, as any large amount of aspirated material is eliminated by coughing.

Very like tuberculosis in childhood, lipoid cell pneumonia gives fewer physical signs than one would expect from the amount of lung involved. Percussion reveals dulness over the affected area, probably masked

somewhat by the overlying normal lung which is free from consolidation and often emphysematous. The breath sounds are usually diminished and bronchial in quality, but they may be harsh, bronchitis being a frequent accompaniment of the condition. Fine or medium moist râles are often heard. There seems to be no significant change in the circulatory system, although cyanosis is occasionally noted. Clubbing of the fingers was present in only one of the cases in this series.

Enlargement of the spleen occurs no more often than would be expected from the coincident infections.

Probably the most valuable aid in the diagnosis of this chronic form of pneumonia caused by aspiration is the roentgenogram.[16] It is by this means alone that one can gain a true idea of the extent of the lesion and a real impression of its chronicity. As can be seen from the accompanying illustrations, the density of the consolidation varies in different parts of the lung, in this respect being more like tuberculosis than lobar pneumonia. Some areas are so dense as to suggest calcification, while immediately adjacent parts of the lung are so little involved as to cast a shadow scarcely heavier than that of normal lungs. As one proceeds peripherally the density of the consolidation decreases. In lateral plates there is more involvement of the posterior than of the anterior part of the lung, a point of great importance. Particularly in the extensive cases there is distinctly a "foreign body" type of distribution, with the right side more affected than the left, the upper more than the lower, and the posterior more than the anterior. It must be remembered that the greatest incidence is in debilitated infants lying constantly on their backs.

Unlike tuberculous infection there is very little enlargement of the mediastinal glands, although a tremendous amount of pulmonary tissue is chronically affected. It is also unusual to see accentuation of bronchial shadows, particularly at the base, as so frequently occurs in chronic interstitial pneumonia. Pleurisy does not occur if there is no acute pulmonary infection with the lipoid pneumonia, and in the cases illustrated not the slightest line of pleural thickening can be seen, although the process in the lungs is an extensive and chronic one. Calcification may occur in the tubercle-like nodules scattered through the area of consolidation; this was demonstrated microscopically in two of the cases.

A single roentgenogram is scarcely ever typical enough to do more than suggest lipoid cell pneumonia. When, however, roentgenograms taken at intervals show little advance or regression of a lesion with the characteristics just mentioned, lipoid cell pneumonia must be seriously considered. This is particularly true in the absence of tuberculosis or of some other known pulmonary infection.

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16. The roentgen changes in cases 1 and 2 were described by J. W. Pierson (Am. J. Roentgenol. **27**:572 [April] 1932).

*Conditions Associated with Lipoid Cell Pneumonia in Twenty-Five Patients*

| Case<br>Patient<br>Date | Age<br>Sex<br>Race | Source | Specific Symptoms | Physical and Roentgen Examination | Complications | Pathologic Report |
|---|---|---|---|---|---|---|
| 1<br>A. P.<br>1929 | 4 mos.<br>M<br>W | Liquid petrolatum in nose and by mouth; cod liver oil by mouth | Cough; rapid respirations; cyanosis, clubbed fingers; failure to gain | Percussion revealed dulness in interscapular region and scattered râles; roentgenogram showed persistent marked consolidation, more on the right | Terminal streptococcic meningitis | "There is some consolidation about the hilus of the left lung; in passing to the right lung there is found to be a very extensive consolidation occupying all the more central part of the lung, leaving some part uninvolved at the apex, base and outer surface; this is a peculiar consolidation, with scar tissue extending out from and around the bronchi and blood vessels, ending sharply against normal looking pulmonary tissue. There are several tubercle-like nodules 2 or 3 mm. in diameter. All of this tissue is found to contain a fatty material which gives the reactions of liquid petrolatum" |
| 2<br>J. P.<br>1930 | 4 mos.<br>F<br>W | Liquid petrolatum daily for two months for constipation; cod liver oil daily; much vomiting | Rapid respirations; cough; failure to gain | Percussion revealed dulness in both upper lobes posteriorly with diminished breath sounds; roentgenogram showed extensive consolidation on both sides coming out from hilus; no change in roentgen report after five weeks | Congenital malformation of kidney with pyonephrosis and uremia | "The lungs are the site of chronic lipoid cell pneumonia with a superimposed lobular pneumonia, so there is a mixture of chronic changes with fresh inflammation; in the areas of lipoid pneumonia the alveoli are distorted and now form wide irregular spaces which are lined with almost cuboidal epithelium; these contain globules of fat; many of these alveoli are partly filled with polymorphonuclears; there is some scarring between the dilated alveoli; there are often dense looking thick bands which contain some scar tissue and in which there are many mononuclear cells filled with fat; some bronchi contain purulent exudate; others are occluded with fat globules and phagocytes loaded with fat" |
| 3<br>E. R.<br>1932 | 3½ mos.<br>F<br>W | Liquid petrolatum for constipation | Rapid, grunting respirations | Percussion revealed dulness and exaggerated breath sounds in interscapular and infraclavicular regions; roentgenogram showed infiltration in both hilar regions | None; condition improved slowly | |
| 4<br>W. B.<br>1929 | 11 mos.<br>M<br>C | Received cod liver oil daily; had long illness during which frequent gavage was done | Symptoms marked by acute pulmonary infection | Both showed acute pneumonia and empyema | Acute pneumonia; empyema; pericarditis; meningitis | Autopsy showed old pleurisy, fresh lobular pneumonia and large areas of lipoid cell pneumonia with mononuclear cells containing fat, giant cells and some polymorphonuclears in the alveoli |
| 5<br>B. M.<br>1930 | 2 mos.<br>F<br>C | Frequent vomiting; had cod liver oil for ten days before death | Cough, rapid respiration | Signs of diffuse bronchitis; roentgenogram suggested tuberculosis | Acute bronchitis; thrush | "The posterior portions of the lung are deep red, bulky and show extensive consolidation; some areas are distinctly yellow; microscopically the lung shows lobular pneumonia, the alveoli being filled with cells of various kinds, but particularly striking are the large mononuclear cells with much vacuolated cytoplasm; the septums are not especially spread apart, as in some cases, by accumulation of fat" |

| | | | | | | |
|---|---|---|---|---|---|---|
| 6<br>D. K.<br>1930 | 16 mos.<br>F<br>W | Vomited often; had cod liver oil regularly; had oil drops in nose | Rapid respirations | Malnutrition and signs of infection of upper respiratory tract | Otitis media; mastoiditis; marasmus; meningitis | Large amount of both chronic and acute lipoid cell pneumonia; many tubercle-like structures around oil, some of which show caseous necrosis and calcification; droplets of oil in bronchi; acute bronchitis |
| 7<br>J. D.<br>1931 | 3 yrs.<br>F<br>W | Comatose for many days; vomited | None | Nothing to indicate consolidation | Aplastic anemia; staphylococcic septicemia | Small amount of pneumonia in lungs due to aspiration of fat |
| 8<br>F. H.<br>1932 | 4 mos.<br>F<br>W | Liquid petrolatum in nose; petrolatum and camphorated oil in nose; castor oil each day | Cough and rapid respiration | Dulness on percussion and occasional râles; roentgenogram showed chronic consolidation on both sides | Congenital syphilis; acute nephritis pneumococcic meningitis | Pleura of lungs smooth; pulmonary substance seems to contain small areas of patchy consolidation which on section show a yellowish lobulation together with a few darker areas; microscopically, it is typically a lipoid cell pneumonia with areas of fresh lobular pneumonia; the bronchial lymph nodes contain fat |
| 9<br>K. A.<br>1932 | 3 yrs.<br>M<br>W | Vomiting when comatose; convulsions | Cough | Dulness and diminished breath sounds at both bases | Severe dysentery with convulsions and coma | Lobular and lipoid cell pneumonia |
| 10<br>R. H.<br>1924 | 3 mos.<br>M<br>W | Vomiting and convulsions | None | None | Otitis media; acute nutritional disturbance | Many alveoli contain large mononuclear cells laden with fat; sometimes the alveoli are plugged with these large cells; several small areas of consolidation |
| 11<br>C. G.<br>1924 | 9 mos.<br>M<br>C | Cod liver oil daily | Cough | Nothing to indicate pneumonia | Congenital syphilis; pneumococcic meningitis and septicemia | Many small scattered nodules of lipoid cell pneumonia, most of them peribronchial; alveoli filled with large cells which frequently are vacuolated as though having contained fat |
| 12<br>M. B.<br>1927 | 3 yrs.<br>F<br>C | Was frequently gavaged while comatose | No symptoms of pulmonary involvement | Lungs clear | Tumor of brain with convulsions and coma | Posterior part of the lower lobes involved; many cells laden with fat seen in the alveoli; there is also a leukocytic pneumonia |
| 13<br>D. M.<br>1926 | 10 mos.<br>F<br>C | Cod liver oil, two teaspoons a day for several months; chronic cough | Frequent respiratory infections and cough | Dulness in upper lobe of right lung; scattered moist râles | Congenital syphilis; streptococcic meningitis | Lower part of upper lobe of right lung is site of firm yellow consolidation; mononuclear phagocytes containing fat are in alveoli and also strands of connective tissue |
| 14<br>W. M.<br>1928 | 2 yrs.<br>M<br>W | Received cod liver oil regularly; frequent vomiting and convulsions | Rapid respiration | Percussion revealed dulness and râles | Congenital cerebral defect; convulsions | Definite areas of lipoid cell pneumonia in which the alveoli contain foamy cells full of fat |
| 15<br>S. S.<br>1927 | 4 mos.<br>F<br>W | Had cod liver oil for three weeks; vomited frequently | None | Dulness and increased breath sounds at left base and right apex | Marasmus; otitis media; furunculosis | In central portion of left lung is consolidated area showing thickening of the alveolar walls and great masses of mononuclear phagocytes filled with fat |
| 16<br>E. L.<br>1930 | 7 yrs.<br>F<br>C | Convulsions, stupor and vomiting | None | Dulness on percussion; roentgenogram shows definite shadow, read as tuberculosis | Pott's disease; pulmonary tuberculosis; tuberculous meningitis | The lungs contain much tuberculosis, but there is a large patch of lipoid cell pneumonia in lower part of upper lobe of right lung |

*Conditions Associated with Lipoid Cell Pneumonia in Twenty-Five Patients—Continued*

| Case<br>Patient<br>Date | Age<br>Sex<br>Race | Source | Specific Symptoms | Physical and Roentgen Examination | Complications | Pathologic Report |
|---|---|---|---|---|---|---|
| 17<br>G. W.<br>1928 | 2 mos.<br>F<br>C | Convulsions; milk and cod liver oil often regurgitated through nose | Cough; rapid respirations | Rapid breathing; harsh breath sounds; cyanosis | Congenital syphilis | "There is a generalized thickening of the alveolar walls; the walls of the small bronchioles are often infiltrated with lymphocytes; many alveoli contain fat-holding phagocytic cells and a few red blood cells and coagulated serum; there is a thickening of the alveolar walls by accumulations of lymphocytes and large mononuclear cells; the polymorphonuclears are also occasionally present" |
| 18<br>W. F.<br>1929 | 5 mos.<br>M<br>C | Vomiting; received some cod liver oil | None | Breath sounds harsh in interscapular region | Dysentery; rickets; malnutrition | The alveolar walls are in places infiltrated with leukocytes and plasma cells, and the alveoli are filled with large vacuolated mononuclear leukocytes containing fat |
| 19<br>J. W.<br>1927 | 14 mos.<br>M<br>C | Vomited | Masked by acute pneumonia | Signs of pneumonia at right base | pleurisy | of the alveoli are accumulations of mononuclear cells the bronchi and some of the alveoli contain masses of older looking exudate partly organized; in many of the alveoli are accumulations of mononuclear cells filled with fat |
| 20<br>J. S.<br>1930 | 5 mos.<br>M<br>W | Convulsions and vomiting with aspiration | None | Lungs clear | Chronic meningitis with convulsions and vomiting | Extensive lobular pneumonia; the alveoli of the lung in places filled with fat-holding mononuclear cells |
| 21<br>M. W.<br>1929 | 3 wks.<br>M<br>C | Unknown | Difficult breathing; pallor | Chest filled with bubbling râles | Gastric hemorrhage | Patchy areas of consolidation in the lower lobe of left lung and middle and lower lobes of right lung; many alveolar septums are thick and infiltrated with mononuclear cells; patchy lipoid cell pneumonia |
| 22<br>L. S.<br>1930 | 2 mos.<br>M<br>W | Vomited frequently | None | No signs | Hydrocephalus with operation; bilateral otitis media | A few patches of pneumonia; more prominent are patches in which the alveolar walls are thickened; alveoli contain large mononuclear cells and there are some polymorphonuclears; frozen section shows large quantities of fat |
| 23<br>J. J. F.<br>1931 | 11 mos.<br>M<br>W | Had small amount of cod liver oil | Cough; rattling in chest, rapid respirations | Rapid respirations; scattered moist râles | Intussusception; typhoid fever (?); operation | Widespread lipoid cell pneumonia and also a fresh lobular pneumonia |
| 24<br>A. F.<br>1931 | 4 yrs.<br>M<br>W | Vomiting | None | None | Tumor of brain (died before operation shortly after admission) | Scattered large globules of fat, mostly in the lymphatics; in places the alveolar walls are swollen and thick with droplets of oil; many bronchial lymph nodes contain fat |
| 25<br>H. B.<br>1928 | 4 yrs.<br>F<br>W | Frequent vomiting | Obscured by those of heart failure | Patient dead when brought in | Rheumatic heart disease with myocardial failure | Lungs show slight chronic passive congestion, but lipoid cell pneumonia is more prominent, with large phagocytic cells containing aspirated droplets of fat |

Some associated illness nearly always brings the patient with lipoid cell pneumonia to the hospital or dispensary. It is useless to enumerate these infections and pathologic conditions, as the series reported here, for example, shows such diversities as simple cold, congenital syphilis, the various forms of meningitis, congenital cerebral defects, tumor of the brain, diarrhea and streptococcic septicemia. The interesting point is that all the children, with one or two exceptions, had some serious illness. On analysis the cases fall into three classes.

The first and largest class is made up of cases of meningitis, tumor of the brain, congenital cerebral defects and severe infections with coma or convulsions. In these the loss of consciousness and diminished cough reflex, as well as the supine position, favor the aspiration of foodstuffs or medicines taken into the mouth or regurgitated from the stomach. Gavage is frequently necessary in the same type of cases. This sometimes results in milk or other food finding its way to the lungs. When it is not coughed up, pneumonia results.

The second type of case is that of very small infants with debilitating disease causing such weakness as to make vigorous coughing impossible. These babies, if not carefully cared for, lie on their backs, and inert nonirritating substances such as liquid petrolatum easily gravitate to the posterior part of the lung. In the third class vomiting is a most conspicuous feature; its cause may be as complex as in case 2 or it may be simply due to improper feeding habits. The conditions associated with lipoid cell pneumonia are given in detail in the table.

The course of the disease is in most cases determined by the condition associated with it. The uncomplicated lipoid cell pneumonia that we have observed has tended to improve. The change is slow, and little difference can be seen in the condition from week to week. Months may elapse before either physical examination or roentgenograms show the pulmonary consolidation to be diminishing. Scarring of the lung must remain for long periods of time after the oil itself has been phagocytosed and carried away. The rapid respirations gradually diminish, and the cough slowly disappears. Stunting of growth is so often associated with the active phase of lipoid cell pneumonia as to make one feel it to be part of the clinical picture.

## PATHOLOGIC PROCESS

There is as great a difference in the pathologic picture found at autopsy in cases of lipoid cell pneumonia, as there is in the clinical picture presented before death. This variation depends on the age of the process, the amount of secondary infection present, the extent of the pneumonia and the type of oil aspirated.

Unless there is a coincident acute pneumonia or empyema the pleura is smooth over the affected areas. The consolidation feels quite firm,

and at times definite nodules can be outlined below the surface of the lung. In the cases in which there is more extensive involvement the lungs feel heavy. On cutting the lung surface the area of the lipoid cell pneumonia varies in appearance. Some of the fresh patches are hemorrhagic and quite red. Other patches are yellow or grayish yellow from the fat and fat-holding cells contained in them. The older areas are apt to be light gray or grayish yellow and to contain much connective tissue. All the areas are firm. The cut surface feels greasy and droplets of fat can often be seen on the blade of the knife. The bronchi are frequently inflamed and may contain droplets of fat. Acute lobular pneumonia is associated with lipoid cell pneumonia in a number of cases.

A striking thing about the gross appearance of the lungs is the close proximity of normal pulmonary tissue to that which is densely consolidated. The involvement tends to be central and posterior, and it is only in the most extensive cases that the peripheral lobules are affected.

The nodules which can be felt below the surface of the lung and seen in cut section look exactly like tubercles, having a fibrous capsule and often necrotic material at the center which is not recognized as fat unless special stains are used. They vary in size, but may be from 1 to 2 cm. in diameter.

The lymph glands are not enlarged in proportion to the amount of lung involved and often are not enlarged at all. They may contain a grayish-yellow infiltration with fat, but rarely contain tubercle-like nodules similar to those found in the lungs.

In microscopic section an acute or subacute bronchitis is almost the rule. With the proper stains globules of oil can often be demonstrated in the bronchi and fat-holding phagocytes can be seen in the lymphatics of the bronchial wall.

The alveoli themselves vary greatly in appearance. They are usually somewhat distorted and often enlarged. The epithelial lining tends to become cuboidal rather than flat, and proliferates many times so that it is composed of several layers of cells. The alveolar spaces may contain free fat, but more often they are packed with large mononuclear phagocytes full of small droplets of oil. Sometimes red blood cells and fibrin are present, and not infrequently polymorphonuclear neutrophils are found in the alveolar exudate. In the alveolar walls themselves, in addition to the types of cells found in the alveolar spaces, there is a great increase in the amount of fibrous tissue, sometimes to such a degree that the septums appear as irregular bands stretching across the lung.

The lymphatics are full of fat-containing phagocytes, and the lymph spaces of the bronchial and mediastinal nodes may be packed with these same cells.

Around the larger masses of fat in the lungs are tubercle-like structures. A globule of oil occupying the center is surrounded perhaps by a small amount of necrotic tissue. There are many giant cells present, outside of which are typical epithelioid cells. A fibrous capsule encloses the whole. Should the fat in the center happen to be cod liver oil, it may take the acid-fast stain, as Pinkerton [13] pointed out. Definite calcification may occur in such structures.

The pathologic observations in this study confirm those of Laughlen [11] and Pinkerton.[15]

## DIAGNOSIS

Uncomplicated lipoid cell pneumonia offers a good prognosis; hence it is important to distinguish it from tuberculosis and other chronic pulmonary conditions, the eventual outlook of which is not so good. It should be suspected in small, debilitated infants who fail to gain and who have a chronic cough or rapid respiration. These symptoms, in the absence of fever, make one particularly suspicious of lipoid cell pneumonia. In all cases tuberculosis must be ruled out. This may be done by raising the amount of tuberculin used in the intracutaneous test to at least 1 and preferably to 5 mg. Examination of the sputum should be of assistance in making the diagnosis of tuberculosis or of fungous or spirochetal disease. In several careful examinations of sputum in two of the cases in this series no fat or fat-laden phagocytes were found.

The blood picture is normal in uncomplicated instances, and is in conformity with the picture of coincident infections. The urine is normal, and physical examination indicates only that there is some sort of pulmonary consolidation present. It is to the roentgenogram that one must turn for the greatest help. It is well to repeat the points mentioned previously. The consolidation is central, bilateral, more extensive on the right and apt to be posterior. The roentgen shadow is always more extensive than the amount of consolidation suspected from physical examination. The process is chronic, and roentgenograms taken weeks apart may show scarcely any difference in the appearance of the lungs. The presence of pleurisy and enlargement of the mediastinal glands favor tuberculosis. Calcification in the pulmonary tissue may occur in either condition, but I have never seen cavitation in lipoid cell pneumonia or calcification in the bronchial lymph nodes.

The abundant foul sputum of pulmonary abscess and bronchiectasis has not occurred in the cases of this type of pneumonia reported here, and the absence of fever would help in differentiation. The tendency for the lesion to disappear gradually makes the picture unlike that of a neoplasm or congenital malformation, and the physical signs are rarely those of atelectasis.

## TREATMENT

Good nursing care with frequent change of position and avoidance of infection of the upper respiratory tract is the only treatment we have at present in use for lipoid cell pneumonia. At the Harriet Lane Home we feel it unwise to use drops of oil in the nose of any small or weak infant, and liquid petrolatum as a cathartic has been given up in the same type of case. When cod liver oil is poorly taken, it seems wise to substitute one of the more concentrated vitamin D preparations.

Among older children it is only in those who are very ill or comatose or in those suffering from some neurologic disorder that we take unusual precautions to prevent aspiration. Care in feeding and gavage done only by experienced persons will repay an institution in the decreased incidence of pneumonia from the aspiration of foodstuffs. When children are inclined to vomit, it is very important that they be placed on the side.

Much work remains to be done in clinical observation of this type of case, and I feel that the recognition of the condition is an aid in solving the problems of the difficult group of chronic nontuberculous pulmonary infiltrations.

Dr. E. A. Park assisted in this study, the Pathological Department of the Johns Hopkins Hospital furnished material, and W. B. Saunders Company gave permission to reproduce figures 4 and 7.

# THE GRASP REFLEX OF THE NEW-BORN INFANT

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The grasp reflex has received considerable attention from neurologists in recent years, particularly in relation to the localization of tumors in the frontal lobe. Knowledge, however, is still limited regarding the exact areas in the brain responsible for the mechanism, and the significance of its appearance in the adult is unknown. It is generally agreed that more light may be thrown on the grasping response seen under pathologic conditions in adults by a thorough investigation of the grasp reflex of the new-born. For this reason several neurologists have recently made studies of this phenomenon in very young children. Most recently, Sittig [1] (1933) and Brain and Curran [2] (1931) extended the investigation to include a study of the grasp response of the feet. Their work was concerned largely with the percentages of infants showing the reflex, the age incidence and a correlation of its disappearance with the development of some voluntary activity, such as fixation, standing or walking. It has been established that the grasp reflex of the hands is present in most, although not in all, new-born infants and that it tends to disappear in children from 5 to 6 months of age, about the time that voluntary grasping and reaching have been established.

In previous studies the presence of the reflex was determined by observation of the response made to a slender rod placed in the baby's hand. This method demonstrated only the presence or absence of the reflex and gave no indication of its strength. I have attempted to carry this work a step farther along the line of Watson's [3] original experiments: first, by putting it on an objective basis, with a method for measuring the strength of the reflex, and second, by obtaining repeated records in the same infant, in contrast to the single observation of previous studies.

The clinging response of new-born monkeys is clearly analogous to the grasp reflex of new-born babies. Histories of the onset, development and disappearance of involuntary clinging have already been obtained

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From the Psychobiological Laboratory, Phipps Psychiatric Clinic, Johns Hopkins Hospital.

1. Sittig, O.: Monatschr. f. Psychiat. u. Neurol. **65**:153, 1933.

2. Brain, W. R., and Curran, R. D.: Proc. Roy. Soc. Med. **24**:869, 1931.

3. Watson, J. B.: Psychology from the Standpoint of the Behaviorist, Philadelphia, J. B. Lippincott Company, 1919, pp. 240 and 276.

in nine new-born monkeys (Richter, 1931).[4] In all these animals the reflex was present at birth, reached its maximum strength between fifteen and forty days later, and then began to decrease. It was not constantly present, however, and showed marked fluctuations from day to day. It disappeared for the most part between the fortieth and fiftieth days, although in one animal it was still present on the eighty-third day, when the investigation was discontinued. It was found, further, that the reflex was much stronger in the infant monkey than in the adult under the influence of drugs [5] or with experimental lesions of the frontal lobe,[6] the reflex lasting for thirty-five minutes in the infant as compared with two minutes in the adult.

With these facts for a basis a similar study has been made on the grasp reflex of the human infant. Through the cooperation of the

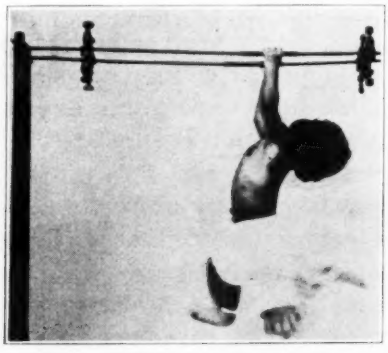

Fig. 1.—Photograph showing new-born infant hanging from apparatus designed to test the grasp reflex.

department of obstetrics of the Johns Hopkins Hospital I have been able to obtain records of thirty-seven infants during their stay in the hospital, many of them from birth to the twelfth day of life and a few up to the twentieth day. It is hoped that in another series of experiments it may be possible to obtain continuous records throughout the first year. The present results will serve as a foundation for such a study.

## METHODS

The technic of measuring the reflex was similar to that employed in the experiments on the new-born monkeys. The apparatus (fig. 1) consisted of two round, parallel brass rods, ¼ inch (0.6 cm.) in diameter, and 5 inches (12.7 cm.) apart, firmly supported 2½ feet (76.3 cm.) above a mattress or a small table. In order to give the infant a firm gripping surface two short pieces of tight fitting, thin

4. Richter, C. P.: Arch. Neurol. & Psychiat. **26**:784 (Oct.) 1931.
5. Richter, C. P., and Paterson, A. S.: Brain **55**:391, 1932.
6. Richter, C. P., and Hines, M.: Am. J. Physiol. **101**:87, 1932.

rubber tubing were placed in the middle of the rods. The infant was held, back down, by the experimenter just beneath the parallel bars, while an assistant brought the palms of the hands into contact with the bars. As soon as the baby gave any indication of grasping, its body was lowered quickly and it was permitted to hang unsupported. The hanging time recorded with a stop-watch served to measure the strength of the reflex.

This method, whereby the infant hangs by both hands rather than by one, has the advantage of eliminating considerable strain, but the hanging time does not seem to be any longer than when the entire weight is supported by one hand.

Robinson[7] (1891), who was the first to study the reflex, and later Watson[3] (1919) used a somewhat different method. They placed the infant on its back and rotated a rod in the palm of the hand to elicit the reflex. When the infant had obtained a good grasp, the rod was raised quickly with the infant hanging on. With this method it is difficult to maintain consistent conditions, since there is always considerable variation in the way the rod is placed in the hand, the speed of lifting is apt to be irregular, and the infant often tends to swing around the supporting arm, thus increasing the strain.

In the present experiments the infants, all Negroes, were tested once each day at approximately the same time, between 10:00 and 11:00 a. m., midway between feedings. Owing to the requirements of routine in the ward it was not possible to obtain records consistently each day, and a number of the infants could not be tested until the fourth or fifth day after birth.

## RESULTS

The results of the experiments are summarized in the table. It can be seen from the data in the fourth and fifth columns that there were great individual differences in the strength of the reflex as measured by the hanging time, the average time ranging from zero to sixty-six seconds, the longest hanging time per infant ranging from zero to one hundred and twenty-eight seconds. Only one of the thirty-seven children failed to hang at any time. The possibility that this one may have shown the reflex had it been tested some days later will be commented on later.

The individual differences are manifest not only in the averages but in the daily records. Three different types of curves are presented in figure 2. The graph in figure 2 *A* shows the daily records of the grasp reflex of an infant from the sixth to the twenty-second day. This type, in which the reflex is weak but fairly constant from day to day, was obtained in several infants. It is probable, however, that had this baby been tested over a longer period it would have shown the type of record seen in figure 2 *B*, in which is shown a definite increase in hanging time after the thirteenth day to a fairly high level of a hundred and twenty seconds. Some of the infants started at once with a strong reflex which showed great daily variation, as may be seen in the curve in figure *C*. These records show how misleading a single observation of

7. Robinson, L.: Nineteenth Cent. **30**:831, 1891.

*The Grasping Reflex in Infants from One to Twenty-Three Days of Age*

| Infant | Age | Number of Records | Average Hanging Time, Sec. | Longest Hanging Time, Sec. | Type of Delivery |
|---|---|---|---|---|---|
| G. A. | 8 days to 23 days | 12 | 60 | 128 | Full term; conservative cesarean |
| G. M. | 6 days to 21 days | 12 | 37 | 110 | Full term; radical cesarean |
| E. G. | 1 day to 8 days | 6 | 66 | 105 | Premature; spontaneous |
| E. F. | 5 days to 6 days | 2 | 49 | 83 | Full term; spontaneous |
| E. D. | 2 days to 10 days | 8 | 27 | 57 | Full term; spontaneous |
| A. M. | 1 day to 8 days | 5 | 33 | 55 | Full term; spontaneous |
| L. W. | 3 days to 8 days | 5 | 17 | 48 | Full term; spontaneous |
| F. S. | 2 days to 7 days | 4 | 18 | 24 | Full term; spontaneous |
| T. T. | 2 days to 7 days | 4 | 14 | 23 | Full term; spontaneous |
| L. P. | 8 days | 1 | 21 | 21 | Full term; spontaneous |
| M. B. | 3 hours to 9 days | 7 | 10 | 20 | Full term; spontaneous |
| M. C. | 3 days to 19 days | 12 | 6 | 20 | Full term; radical cesarean |
| B. T. | 5 days to 9 days | 3 | 14 | 19 | Full term; spontaneous |
| E. P. | 6 days to 22 days | 12 | 10 | 18 | Premature; spontaneous |
| E. H. | 4 days to 9 days | 3 | 10 | 18 | Full term; spontaneous |
| M. O. | 5 days to 12 days | 6 | 8 | 16 | Full term; operative |
| R. McI. | 2 days to 9 days | 4 | 12 | 14 | Full term; spontaneous |
| B. J. | 5 days to 9 days | 2 | 12 | 14 | Full term; spontaneous |
| S. W. | 3 hours to 8 days | 7 | 11 | 14 | Full term; spontaneous |
| L. S. | 2 days to 8 days | 4 | 8 | 14 | Full term; spontaneous |
| M. H. | 9 days | 1 | 11 | 11 | Full term; spontaneous |
| C. S. | 3 hours to 7 days | 7 | 4 | 10 | Full term; spontaneous |
| E. K. | 2 days to 9 days | 5 | 6 | 9 | Full term; spontaneous |
| V. H. | 3 hours to 9 days | 7 | 4 | 9 | Full term; spontaneous |
| L. S. | 3 days to 7 days | 2 | 6 | 8 | Full term; spontaneous |
| E. P. | 3 days to 7 days | 3 | 3 | 8 | Full term; spontaneous |
| P. P. | 3 hours to 7 days | 4 | 4 | 8 | Full term; cesarean |
| C. J. | 1 day to 8 days | 5 | 3 | 7 | Full term; spontaneous |
| E. H. | 10 days | 1 | 7 | 7 | Full term; spontaneous |
| M. D. | 18 days | 1 | 6 | 6 | Full term; cesarean |
| E. H. | 11 days to 12 days | 2 | 6 | 6 | Full term; spontaneous |
| B. C. | 3 hours to 7 days | 7 | 1 | 6 | Full term; spontaneous |
| F. M. | 1 day to 8 days | 4 | 3 | 5 | Full term; spontaneous |
| A. W. | 1 day to 9 days | 6 | 2 | 4 | Full term; spontaneous |
| A. C. | 5 days to 9 days | 2 | 2 | 3 | Full term; operative |
| C. C. | 5 days to 6 days | 2 | 1 | 1 | Premature; spontaneous |
| V. H. | 1 day to 8 days | 6 | 0 | 0 | Full term; spontaneous |

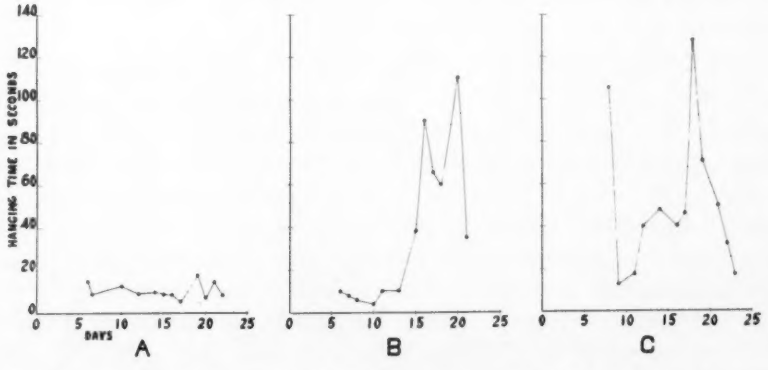


Fig. 2.—Graphs showing individual differences in the daily records: *A*, record of a weak but constant reflex in an infant from the sixth to the twenty-second day; *B*, an increase to a high level in the hanging time after the thirteenth day; *C*, record of a strong reflex showing great daily variation.

the grasp reflex might be, since under these circumstances the examination might be made either on a day when the reflex is small or absent altogether or on a day when it happens to be very active.

It is evident that the grasp reflex of the new-born human infant has in common with the reflex of the baby monkey great individual variation, marked daily fluctuation and a tendency to be relatively inactive for an appreciable interval after birth before attaining a maximum.

It is worthy of note that the involuntary hanging time of human infants has about the same duration as the voluntary hanging time of human adults. For normal adults tested in this laboratory the best hanging record was two and a half minutes. Robinson, in the earliest experiments, reported a hanging time for new-born infants not greater than two minutes, and my own research has given essentially the same result.

## COMMENT

In the experiments reported great individual differences in the strength of the reflex were found. Several attempts have been made to account for these differences. They may be explained, in part, by the fact that the records were not taken for the same length of time on all the infants; it is possible that the reflex may not approach a maximum in many babies until after the first twelve days. Only continuous records from birth to the time of disappearance of the reflex will settle this question. In the meantime it seems that with this factor taken into full account there are still large individual differences to be explained. In some instances there seemed to be a correlation between the strength of the reflex and the responsiveness of the infant (whether partly asleep or not), but this correlation was not consistent. As it is known that the reflex may appear in adult monkeys in conditions characterized by a depression of the nervous system,[5] it seemed worth while to investigate any possible relationship between the strength of the reflex and the type and condition of birth, whether difficult or prolonged, with or without injury. This also failed to yield data of any significance, except that the two longest hanging records belonged to infants delivered through a cesarean section.

The possibility was considered that the marked individual differences in the grasp reflex might have no more significance than differences in the knee jerk, as many healthy persons, active adults as well as infants, show no knee jerk or only a weak one. When the grasp reflex is considered in its biologic setting, however, it seems unlikely that those differences can be explained on any such simple basis. The reflex plays too important and vital a part in the life of the monkeys. Their survival depends largely on it, as the mother does little to support the new-born baby while she jumps about in the trees. Without the aid of a strong clinging reflex the infant would fall to the ground at once.

It may be that the human race is so far removed from its arboreal ancestor, if indeed it ever had one, that this reflex no longer has any significance. The fact that new-born monkeys hang so much longer than adult monkeys while human infants hang only about as long as human adults may be interpreted as indicating that the hanging mechanism is not so important in the human species. However, from what knowledge there is at hand it would seem likely that an infant with a strong grasp reflex would also have the other accompaniments of a more vital organism. The whole question is complicated by the fact that when the reflex is present in older children, it has a negative significance and indicates some retardation in development or some actual injury to the nervous system.

SUMMARY

1. A technic is described for measuring the grasp reflex in the human infant. This technic consists in measuring the length of time the babies hang unsupported from a pair of parallel bars.

2. Records for thirty-seven new-born infants are presented; most of the data were obtained during the first twelve days, but a few as late as twenty days after birth.

3. The records show: (1) Reflexes were present in all but one of the thirty-seven subjects; (2) there were large individual differences and (3) great daily fluctuations, and (4) the reflex was not strongest just after birth, but seemed to reach its highest point after the twelfth day.

# ECZEMA VACCINATUM

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Vaccinia or cowpox resulting from auto-inoculation in a vaccinated person is rather infrequent and usually tends to be benign even in the generalized form. The same disease superimposed on infantile eczema, although rare, is far more serious and usually proves fatal when the face is involved. It may result from direct contact with the virus and is easily confused at first with variola and impetigo. Cases have been reported by Hoffman, Finkelstein, Kiezling, Kobrak, Danzigea, Jerome, Meyer, Swoboda, Eichoff and Hegeler.

The fatal case reported here is of interest from the standpoint of differential diagnosis and should emphasize the importance of surgical asepsis in vaccination against smallpox in children. It afforded an opportunity for bacteriologic investigation of tissues following clinical evidence of encephalitis.

## REPORT OF A CASE

R. V., a white boy, aged 5 months, was admitted to the hospital because of fever, restlessness and facial eczema which had become pustular and swollen during the past two days. He was breast fed and except for a simple eczema he had previously been well. The mother had rheumatic heart disease and was thought to have tuberculosis. There was no history of vaccination or exposure to contagious disease. On admission there was facial eczema with swelling and redness in the left preauricular region. Three or four superimposed papulopustular lesions 8 mm. in diameter with excoriated tops were present. There was moderate bilateral anterior cervical lymphadenopathy, and the temperature was 101 F. Routine examinations of the blood and urine, Mantoux, Wassermann and Kahn tests and a roentgen examination of the chest and long bones gave negative results.

During the next three days the lesions spread over the entire face, involving the cheeks, lips, nose, tip of the tongue and forehead. The temperature rose to 104 F. Confluent grayish-white pustules with raised indurated borders and thick, tough coverings, in the center of which were small central depressions, developed. A biopsy specimen of the lesions was taken, and a blood culture was made. The tentative diagnosis of impetigo was changed to vaccinia, and repeated questioning revealed that the 3 year old brother had been vaccinated two weeks prior to the appearance of the swelling and the purulent exudate on the patient's face. The infant was no doubt infected with the virus derived from the brother's uncovered vaccination wound.

Coincident with a spread of the lesions into the scalp and mouth the child's general condition became worse. He was stuporous during the next ten days and required feeding by tube. Slight strabismus developed. A specimen of the spinal fluid taken at this time was normal. Following transfusion the patient seemed to improve, the lesions were involuting, and the temperature receded to 101 and 102 F., although he was still stuporous. On the fourteenth day dyspnea, hyperpyrexia and abdominal distention developed, and he died twenty-four hours after signs of pneumonia appeared.

From the Department of Pediatrics, University of Minnesota.

Autopsy revealed bronchopneumonia, eczema, vaccinia and cervical lymphadenitis. The brain showed nothing macroscopically. Cultures taken from the skin, spinal fluid and blood remained sterile. The brain was removed for further examination in the department of bacteriology.

Brain tissue weighing about 10 Gm. was taken from the posterior part of the cerebrum and ground in 50 per cent glycerol to make a 20 per cent suspension. Culturing the brain tissue yielded a pure culture of a streptococcus. The glycerolated brain tissue injected intracranially into rabbits produced death in from twenty-four to forty-eight hours, with obvious involvement of the central nervous system.

Photograph showing lesions of vaccinia in an accidentally inoculated infant with symptoms of postvaccinal encephalitis.

Two rabbits inoculated intracerebrally with a Mandler filtrate of the glycerolated suspension died on the seventh and fourteenth days, respectively.

While this result indicates that the virus of smallpox may have been present, the presence of streptococci and the possibility of the occurrence of filtrable forms of this organism make a positive identification of the etiologic agent indecisive.

## CONCLUSION

Experience with this case indicates that there are certain reasons for applying a protective dressing over vaccinated areas in children. It decreases the risk of cross-inoculation of nonvaccinated associates and prevents the child from revaccinating or infecting itself in the act of scratching. It seems also that extreme caution should be used in vaccinating young infants who have open cutaneous lesions.

# Case Reports

## ANEMIA OF THE NEW-BORN WITHOUT ERYTHROBLASTOSIS

### OBSERVATIONS AT AUTOPSY

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MAURICE MORRISON, M.D.

AND

DAVID A. MEYER, M.D.

BROOKLYN

The subject of anemia of the new-born has recently taken on a new interest. Finkelstein [1] (in 1911) and Lichtenstein [2] (1917) first drew attention to the possible occurrence of anemia in the new-born. Ecklin [3] (1919), however, was the first to report "a case of severe anemia in the new-born." Following this, cases have appeared under the titles of idiopathic, primary, essential and congenital anemia. Pritchard and Smith [4] (1931), in a careful survey of the literature, tabulated fifteen cases and mentioned fourteen additional cases observed though not described by Grulee, Foote, McClelland and Blackfan et al. Abt [5] (1932) analyzed the reported cases and presented a case of his own which also showed a mononuclear erythrophagocytosis in the circulating blood. Diamond, Blackfan and Baty [6] (1932) added six cases and concluded that universal edema of the fetus, icterus gravis neonatorum and anemia of the new-born are closely related and that they are dependent on the same underlying pathologic process—erythroblastosis.

Because our infant did not reveal erythroblastosis, we thought it advisable to place this case on record. Similar reports, we hope, will

From the Departments of Pediatrics and Pathology of the Jewish Hospital of Brooklyn.

1. Finkelstein, H.: Berl. klin. Wchnschr. **48**:1829, 1911.

2. Lichtenstein, A.: Abstracted by Denzer, B. S.: Arch. Pediat. **43**:741, 1926.

3. Ecklin, T.: Monatschr. f. Kinderh. **15**:425, 1919.

4. Pritchard, E., and Smith, J.: Case of Severe Anemia in New-Born Infant, Arch. Dis. Childhood **6**:325 (Dec.) 1931.

5. Abt, A.: Anemia of the New-Born, Am. J. Dis. Child. **43**:337 (Feb.) 1932.

6. Diamond, L. K.; Blackfan, K. D., and Baty, J. M.: Erythroblastosis Fetalis and Its Association with Universal Edema of Fetus, Icterus Gravis Neonatorum and Anemia of Newborn, J. Pediat. **1**:269 (Sept.) 1932.

ultimately assist in a better understanding of the underlying pathogenesis and result in a more accurate classification of such cases.

## REPORT OF CASE

*History.*—M. W., a normal white female infant, was born at term on June 17, 1932, following a short uneventful labor and spontaneous delivery. The father and mother were always in good health and serologic tests were negative for

Fig. 1.—A section of liver from a case of universal edema of the fetus with erythroblastosis, showing the extensive islands of extramedullary hematopoiesis. The hepatic architecture is lost, owing to the diffuse involvement by the islands. The process resembles that of leukemic infiltration.

syphilis. The mother had three previous pregnancies; the first gestation (1919) was ended in the fourth month by a therapeutic abortion on account of preeclamptic symptoms; the second (1921) and third (1925) resulted in the birth of two normal children who were living and well. Throughout this fourth pregnancy the mother felt well and presented no toxic symptoms. Her diet was well balanced, including eggs, meats, vegetables, fruits and milk.

At birth the infant weighed 7 pounds and 7 ounces (3,373.6 Gm.), was well developed and cried spontaneously. The mother's breast feedings were complemented by a mixture of three quarters milk, water and dextrimaltose. After a loss of 5 ounces (175.1 Gm.) during the first three days, the child gained steadily, weighing 7 pounds and 5 ounces (3,316.9 Gm.) by the eighth day.

On the sixth day (June 22), it was noticed that the child was pale. Otherwise she seemed normal. There was no icterus or evidence of bleeding from the skin

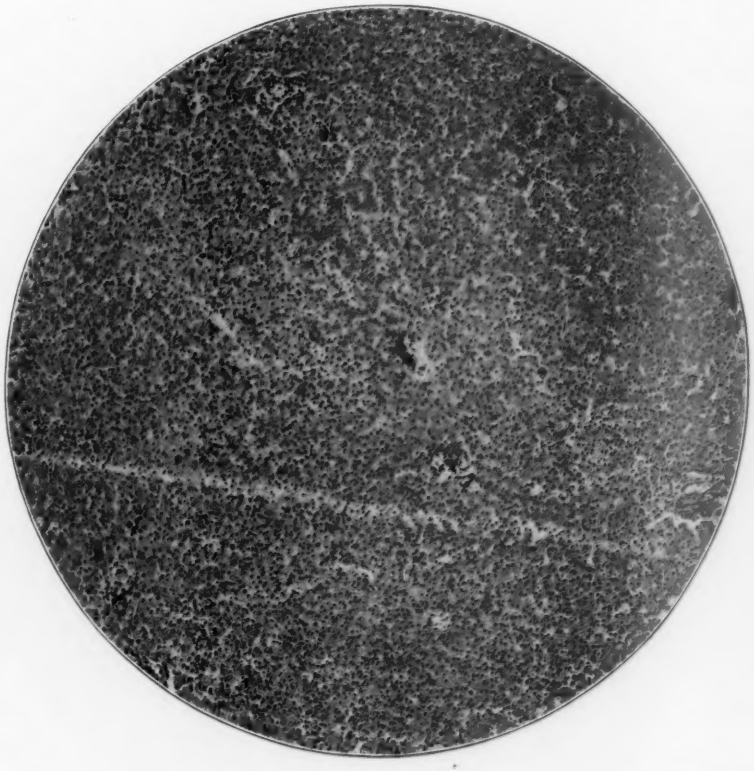

Fig. 2.—A section of liver from the case presented. The absence of islands of hematopoiesis is in marked contrast to the hematopoiesis found in figure 1.

or mucous membranes. The stool was formed and yellow, and it contained no macroscopic blood. The infant was vigorous, cried and nursed well. The red blood cells numbered 2,500,000, and the hemoglobin was 50 per cent (Sahli).

The following day revealed an increased pallor. The heart and lungs were normal. The liver extended two fingerbreadths below the right costal border. The spleen could be felt high under the left costal arch. There was no glandular enlargement. The child's general condition was considered to be good, and the temperature was never elevated.

*Study of Blood.*—On the eighth day (June 24), 25 cc. of the father's whole blood was injected intramuscularly into the buttocks. Immediately before this

procedure examination of the blood showed the following: erythrocytes, 1,380,000; leukocytes, 60,000; hemoglobin, 20 per cent (Dare); color index, 0.79 per cent; platelets, 250,000; bleeding time, one minute; coagulation time, five minutes (capillary tube). Clot retraction began in one-half hour and was complete in ten hours. The tourniquet test showed normal results. Differential study of the leukocytes (400 cells) showed: neutrophils, 22.5 per cent (segmented); neutrophils, 16.0 per cent (band forms); eosinophils, 1.0 per cent; basophils, 0.5 per cent; lymphocytes,

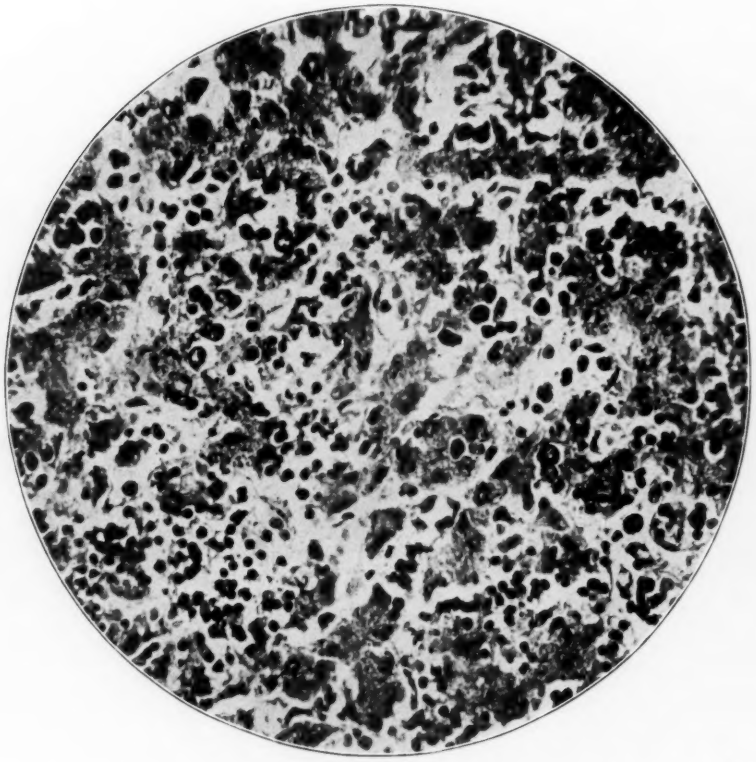

Fig. 3.—High power magnification of figure 1, showing the islands of hematopoiesis compressing and replacing the hepatic cells, which are undergoing vacuolization. The foci of hematopoiesis are in the sinusoids and periportal spaces. Although numerous myeloid cells are present in the islands, the majority of the cells are erythroblasts and immature red cells in various other stages of development.

35.5 per cent; monocytes, 2.5 per cent; lymphoblasts, 0.5 per cent; myeloblasts, 1.0 per cent; myelocytes, 6.0 per cent; metamyelocytes, 15.0 per cent.

Study of the red cells revealed 6 normoblasts to 200 white cells counted. There were slight anisocytosis, hypochromasia, anochromasia and macrocytosis and moderate polychromasia and microcytosis. Reticulation was 0.5 per cent. Hemolysis began in 0.36 per cent saline solution and was still incomplete in 0.28 per cent

saline solution, showing an increased resistance. Blood for the Wassermann test was hemolyzed.

Because of the blood picture it was decided to give the infant a transfusion of blood despite its fairly good general condition. Before this could be accomplished, the child suddenly became extremely pale and breathed irregularly. The heart sounds were only faintly heard. Saline solution was injected into the veins with no response. Twenty cubic centimeters of blood from a professional donor was

Fig. 4.—High power magnification of figure 2 showing the relatively unchanged hepatic tissue, in marked contrast to the changes in the corresponding section from the case of erythroblastosis shown in figure 3.

then injected into the vein, but the child died (June 25) at the end of this procedure.

*Autopsy* (by Dr. S. H. Polayes).—The body was that of a full-term infant, 9 days of age. The striking feature of the external examination was the severe anemia of the skin and mucous membranes. The peritoneal cavity was normal except for a small quantity of clear yellow fluid. The pleural and pericardial cavities were normal.

The heart weighed 22 Gm.; the epicardium, myocardium and endocardium, including the valves, were normal. The foramen ovale was widely patent, and

the ductus arteriosus was patent. The coronary arteries were normal. Microscopic examination revealed no changes other than anemia. The aorta was normal.

The thymus weighed 6 Gm. and showed no changes. The trachea and bronchi were normal except for the anemia.

In the lungs the pleural surfaces were smooth and glistening, and the consistency was normal throughout. The cut section showed congestion. The lung was the only organ in which congestion could be demonstrated. The pulmonary vessels stood out prominently. Microscopic examination revealed the blood vessels to be

Fig. 5.—A section of the spleen from the case of universal edema of the fetus with erythroblastosis, showing the extensive extramedullary hematopoiesis destroying the normal architecture. The splenic follicles have lost their prominence, and active hematopoiesis is found throughout the section. Immature red cells in various stages of formation are found in great abundance.

congested, in contrast to the other organs. The section cut through the lower lobe of the right lung showed an atelectatic condition of the pulmonary tissue; the section through the lower lobe of the left lung showed edema of the alveoli and interstitial thickening of the interalveolar septums. The architecture of the tracheobronchial lymph nodes was altered by marked edema. There were numerous spaces containing immature blood cells of the granulocytic series.

The liver weighed 180 Gm. The surface was smooth and pale and the consistency was normal. Section showed a pale and clouded cut surface. The biliary channels and portal vessels were normal. Microscopic examination of the hepatic cells showed degeneration of the cytoplasm. The May-Grünwald stains failed to show an increase in the number or size of the islands of hematopoiesis, and there was no increase in the erythroblasts. The gallbladder was filled with light-colored fluid bile which could easily be expressed through the cystic and common ducts. The pancreas showed severe anemia.

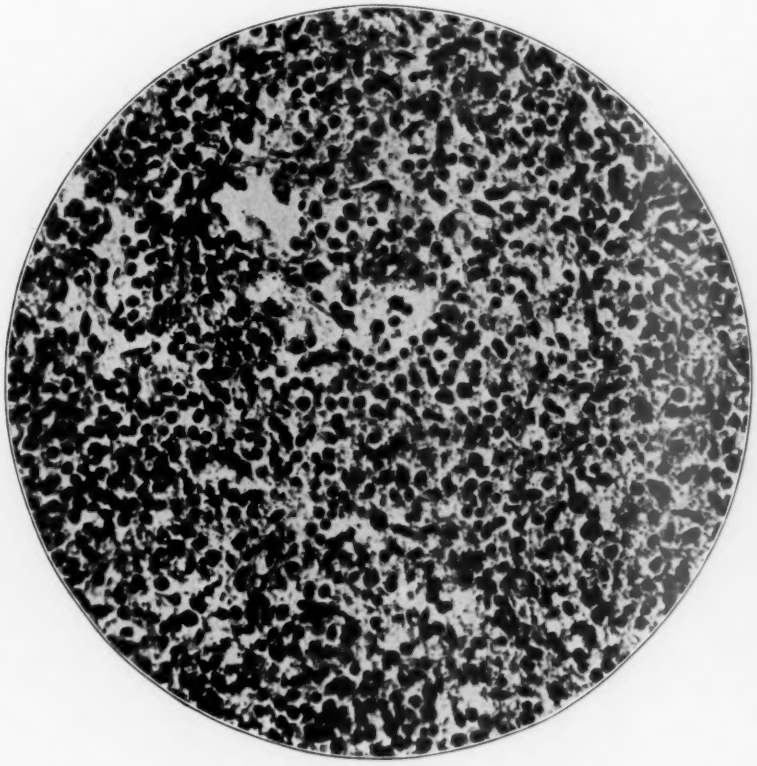

Fig. 6.—A section of the spleen from the case presented. The architecture of the splenic pulp and sinuses is well preserved in contrast to the changes noted in figure 5 in which the architecture is destroyed by marked hematopoiesis.

The stomach and intestines showed no changes other than those caused by anemia, and the mesentery was normal, except for moderate hyperplasia of the lymph nodes. Microscopic examination revealed the intestines to be normal.

May-Grünwald stains of the mesenteric lymph nodes showed an increase in the number of eosinophils.

The spleen weighed 10 Gm. The cut section showed a fairly normal architecture except for pallor. The splenic vessels were normal. An accessory spleen

was found, measuring 2 cm. in diameter and similar to the main spleen. On microscopic examination the splenic follicles were not prominent, and there was no marked increase in the number of hematopoietic centers.

The suprarenal glands each weighed about 1.5 Gm. The cut section showed no changes grossly or microscopically.

The kidneys each weighed about 12 Gm. The capsules stripped with ease, leaving a smooth but congested surface. The cut section showed a clouding of

Fig. 7.—A section of the kidney from a case of erythroblastosis, cut through the zone between the cortex and medulla, showing extremely active foci of hematopoiesis, some of which are periglomerular in distribution.

the parenchyma. Microscopic examination of the sections showed normal fetal structure of the cortex and medulla. There were no islands of hematopoiesis present. The ureters and bladder and the genitalia were normal.

The scalp and cranial bones were normal. The meninges were congested and the brain was edematous and congested. The pituitary gland was normal. Microscopic examination of the sections showed no changes.

Examination of the bones revealed a normal amount of dark red marrow present in the ribs. The epiphyses of the tibia and femur were normal. The marrow was red and fairly dry. Microscopic examination of the bone marrow showed

definite hyperplasia of the granulocytic element, with a proportional increase in the number of eosinophils. There was no evidence of increase in erythroblasts.

The blood exuding from the large vessels of the neck at autopsy, when collected in a test tube, revealed a very small proportion of red cells to plasma, about 1 : 8. The plasma was a turbid yellow.

The anatomic diagnosis was: congenital anemia; partial pulmonary atelectasis and edema; cloudy swelling of the viscera; cerebral edema; an accessory spleen, and hyperplasia of the bone marrow.

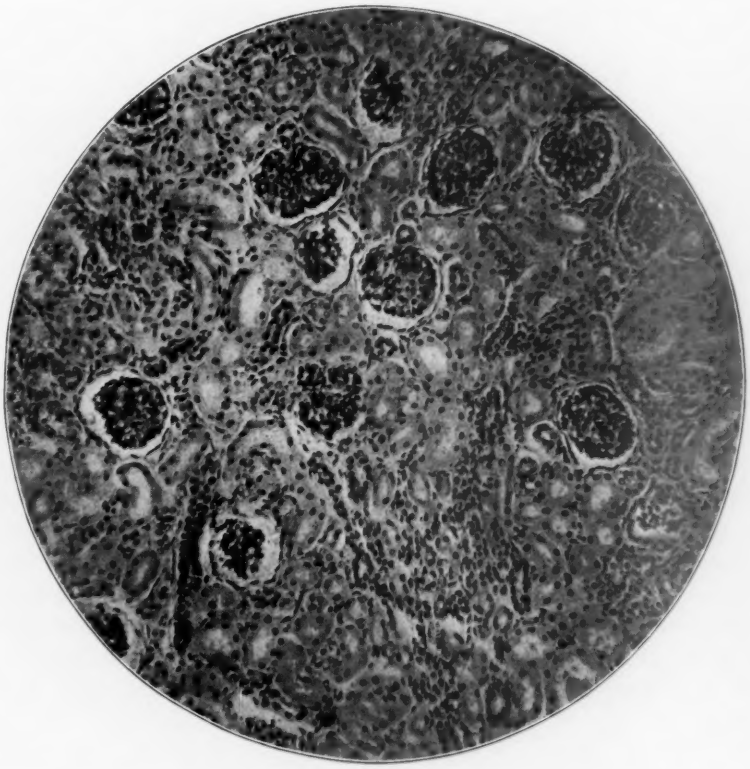

Fig. 8.—A section of the kidney from the case presented, cut through the zone corresponding to that of figure 7, showing no foci of hematopoiesis.

## COMMENT

We have thus described a case of anemia in a new-born child, accompanied by hyperactivity of the myeloid tissue, as evidenced by a high leukocytosis with a moderate shift to the left. The shift to the left consisted of immature myeloid cells, myelocytes, metamyelocytes and band forms. The slight increase in normoblasts and polychromasia are evidence of regeneration of red cells.

The anemia became progressively worse, finally ending in collapse and death before transfusion could be of benefit. A similar crisis

occurred in the case described by Pasachoff and Wilson.[7] In both instances it is not unlikely that transfusion would have been a life-saving measure. We believe, therefore, that transfusion should be done in all severe cases and in every apparently mild case in which the blood picture is becoming worse. There is evidently no warning of the approaching collapse.

The anemia in this case must not be confused with anemia which is secondary to hemorrhage, hemorrhagic disease of the new-born, active congenital syphilis, hemolytic icterus, prematurity, sepsis, aplastic anemia or leukemia. The absence of a tendency to bleeding, general glandular enlargement, icterus or fever, the increased resistance of the red cells to hypotonic saline solution, the lack of syphilitic stigmas, the negative results of blood tests in the parents and the absence of pathologic processes indicative of the aforementioned conditions serve to exclude them as etiologic factors. The partial pulmonary atelectasis is probably an incidental finding, while the cloudy swelling of the viscera and the cerebral edema are most likely secondary to the anemia.

Grulee [8] was among the first to suggest the possible relationship between anemia of the new-born and erythroblastosis. Recently, there has been an attempt to correlate universal edema of the fetus, familial icterus gravis neonatorum and anemia of the new-born. Diamond, Blackfan and Baty [6] firmly believe that despite the differences in clinical manifestations, these diseases are dependent on the same underlying disturbance of the hematopoietic system, namely, erythroblastosis. The association of universal edema of the fetus and familial icterus gravis neonatorum with erythroblastosis seems definite.[9] However, further evidence is necessary before all cases of anemia of the new-born can be included in this category. In cases of anemia of the new-born presented by Diamond, Blackfan and Baty recovery took place, and there was, therefore, no pathologic confirmation of erythroblastosis in the tissues.

In our patient, on the other hand, a careful search of all the tissues available for study failed to reveal the degree of extramedullary hematopoiesis characteristic of erythroblastosis. The same is true in Pasachoff and Wilson's [7] case. Unfortunately, placental studies were not made in either instance. The presence or absence of extensive erythroblastosis in sections of the placenta would determine whether the anemia

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7. Pasachoff, H. D., and Wilson, L.: Congenital Anemia of the New-Born, Am. J. Dis. Child. **42**:111 (July) 1931.

8. Grulee, C. G., and Bonar, B. E.: The Newborn, Diseases and Abnormalities, New York, D. Appleton and Company, 1926.

9. Ferguson, J. A.: Erythroblastosis with Jaundice and Edema in the Newly Born, Am. J. Path. **7**:277, 1931.

in question is secondary to an erythroblastic process [10] or is dependent on an as yet undiscovered etiologic factor. However, it is fair to assume that the placenta would probably show no greater erythroblastic activity than was found in the other extramedullary organs examined. The available evidence, therefore, makes one agree with the statement made by Clifford and Hertig [11] "that it is for future studies to prove whether idiopathic anemia is an independent entity or whether it is one stage or phase of the erythroblastic process."

SUMMARY

1. A case of severe anemia in a new-born infant is presented, with observations at autopsy.

2. The etiology of the anemia is obscure.

3. Postmortem studies failed to reveal evidences of erythroblastosis.

4. Studies of the placenta in such cases may aid in shedding light on the relationship of anemia of the new-born to familial icterus gravis neonatorum and universal edema of the fetus.

8301 Bay Parkway.

250 Ocean Parkway.

205 Hicks Street.

10. Personal communication from Dr. L. K. Diamond.

11. Clifford, S. H., and Hertig, A. T.: Erythroblastosis of New-Born, New England J. Med. **207**:105 (July 21) 1932.

# XANTHOMATOSIS WITH INVOLVEMENT OF A VERTEBRAL BODY

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While the "punched-out" areas found on roentgenograms of the skull produced by lipoid infiltrations of the reticulo-endothelial system have been reported many times, roentgen evidence of the course of an analogous lesion of the spine with clinical findings of xanthomatosis has not been reported in the literature. The present report is of twofold interest in that such a lesion was found and that the patient apparently recovered completely without special treatment. It is of further interest from a diagnostic standpoint. Schüller [1] (1915) and Christian [2] (1920) described associated exophthalmos and diabetes, now believed to be complications as the result of nonsupporting soft lipoid deposits in the skull. Until Rowland's [3] illuminating descriptions many cases of xanthomatosis were thought to be malignant tumors [4] or tuberculosis. Hand [5] in 1893 was the first to describe a case fitting the Schüller-Christian syndrome, but the pathologic changes were mistakenly reported as due to tuberculosis. Likewise, in the case report here the early histologic interpretation favored myeloma and the clinical diagnosis was Pott's disease.

## REPORT OF A CASE

L. K., a white boy, aged 5 years, came to the Children's Memorial Hospital on Jan. 23, 1924, because of pain in the midportion of the back of one month's duration. The pain, while not constant, was so severe at times that he cried out on

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From the Children's Memorial Hospital.

1. Schüller, Arthur: Ueber eigenartige Schädeldefekte im Jugendalter, Fortschr. a. d. Geb. d. Röntgenstrahlen **23**:12, 1915.

2. Christian, H. A.: Defects in the Membranous Bones, Exophthalmus and Diabetes Insipidus: An Unusual Syndrome of Dyspituitarism, M. Clin. North America **3**:849 (Jan.) 1920.

3. Rowland, R. S.: Xanthomatosis and the Reticulo-Endothelial System, Arch. Int. Med. **42**:611 (Nov.) 1928; Christian's Syndrome and Lipoid Cell Hyperplasia of the Reticulo-Endothelial System, Ann. Int. Med. **2**:1277, 1929.

4. Berkheiser, E. J.: Multiple Myelomas of Children, Arch. Surg. **8**:853 (May) 1924.

5. Hand, A.: Defects of Membranous Bones, Exophthalmus and Polyuria in Childhood: Is It Dyspituitarism? Am. J. M. Sc. **162**:509 (Oct.) 1921.

movement of his body. He had not walked since January 3, when the pain came on suddenly and he refused to stand without support. While in bed he clung to his knees during the attacks of pain. "Lumps" on the head had been noticed since September 1923, but there was no history of injury. There had been several slightly raised areas which had been tender to pressure. Members of the family had noticed that three of these nodules had disappeared, but ten were still palpable on admission to the hospital. Urination had been frequent, and the child had to get up regularly three or four times at night.

The early history gave no clue as to a probable postnatal etiologic factor. The birth had been uncomplicated and occurred at term. He had been breast fed and

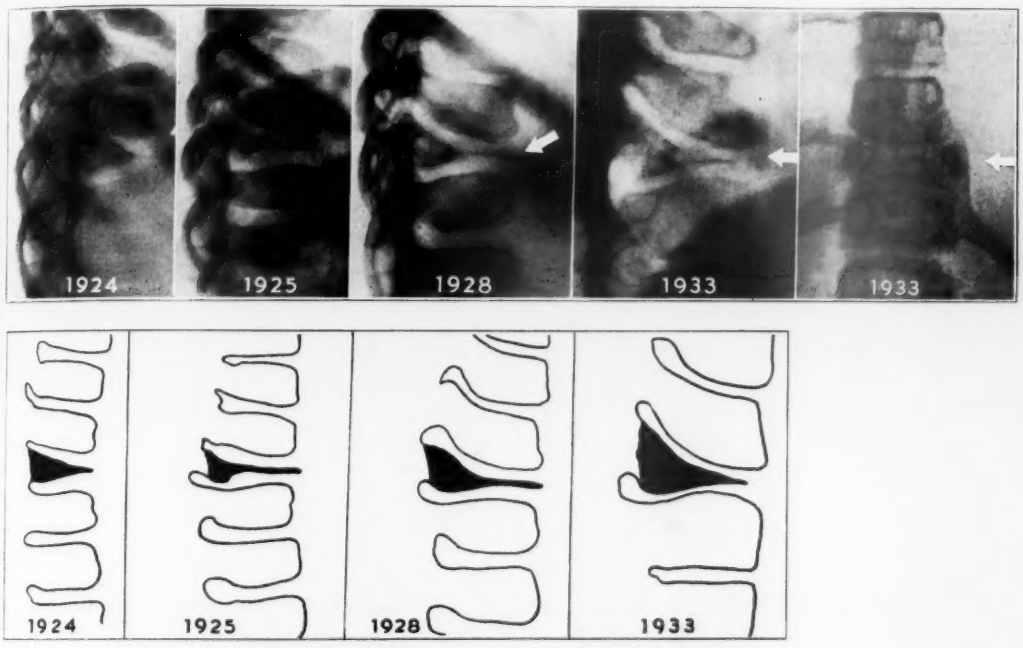


Fig. 1.—Serial roentgenograms of the tenth dorsal vertebra taken at the time noted on the illustrations, corresponding to the roentgenograms of the skull (fig. 2). Note the gradual disappearance of all but the cartilaginous plates without involvement of the intervertebral disks (see tracings) and the regeneration of the body with compensatory overgrowth of the adjacent vertebral bodies without the kyphosis usually seen in tuberculosis.

seemed to develop normally. The first tooth appeared at 8 months. The patient started to talk at 1 year and walked at 14 months. The father stated that the child had had whooping cough at 10 weeks, bronchitis at 9 months and occasional attacks of tonsillitis more recently. The father, mother and three brothers and sisters were living and well. No other members of the family had had dorsal trouble or lumps on their heads. The family history was irrelevant, and so far as could be ascertained, there was no history of contact with tuberculosis. The social service department had reported that the home surroundings were favorable.

Physical examination at the time of admission showed a fairly well developed and well nourished boy who did not appear ill. Slight kyphosis was noted, and there was tenderness over the region of the tenth dorsal vertebra. The back was rigid with marked muscular spasm, and the pain was greater when the child attempted to straighten up. The nodules on the head varied in size, some appearing to be as much as 3 cm. in diameter. They were described as "fairly soft," and

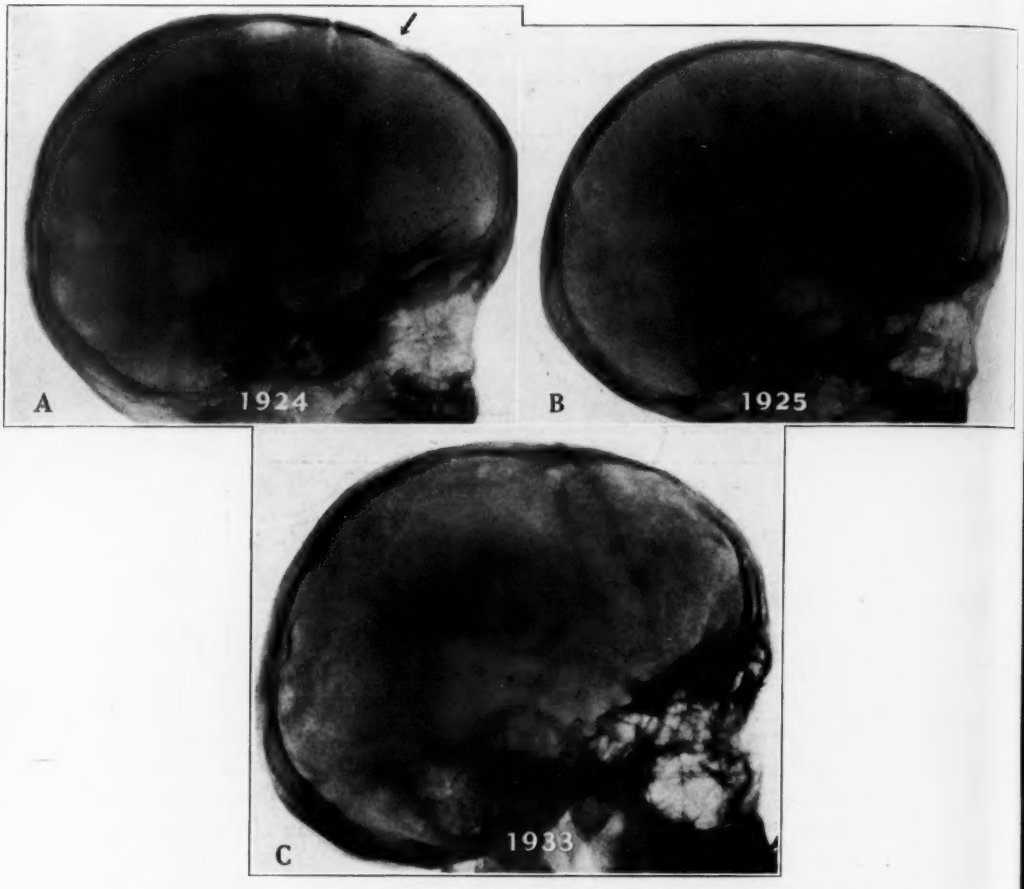


Fig. 2.—*A,* many defects are still present in the skull although some that were formerly palpable have disappeared. The arrow indicates the site of the biopsy. *B,* appearance one year later. All the "punched-out" areas have disappeared. Intervening roentgenograms showed that they were almost gone in six months. *C,* roentgenogram of the skull at the end of nine years. There has been no recurrence of the lesions.

they "seemed to fluctuate." The chest was of the long narrow type. There were many decayed teeth. The temperature had been elevated less than a degree at times, but it was normal most of the time.

The roentgenogram of the spine (fig. 1) showed a narrowing of the tenth dorsal vertebral body. The normal appearing intervertebral disks above and below appar-

ently made contact anteriorly, enclosing a straight-edged wedge-shaped body of normal density. A note at that time stated: "The edges are clearcut and rather smooth and do not appear typical of tuberculosis."

A roentgenogram of the skull (fig. 2) showed ten oval areas of decreased density. The largest measured 2 by 3 cm. in diameter. They appeared "punched

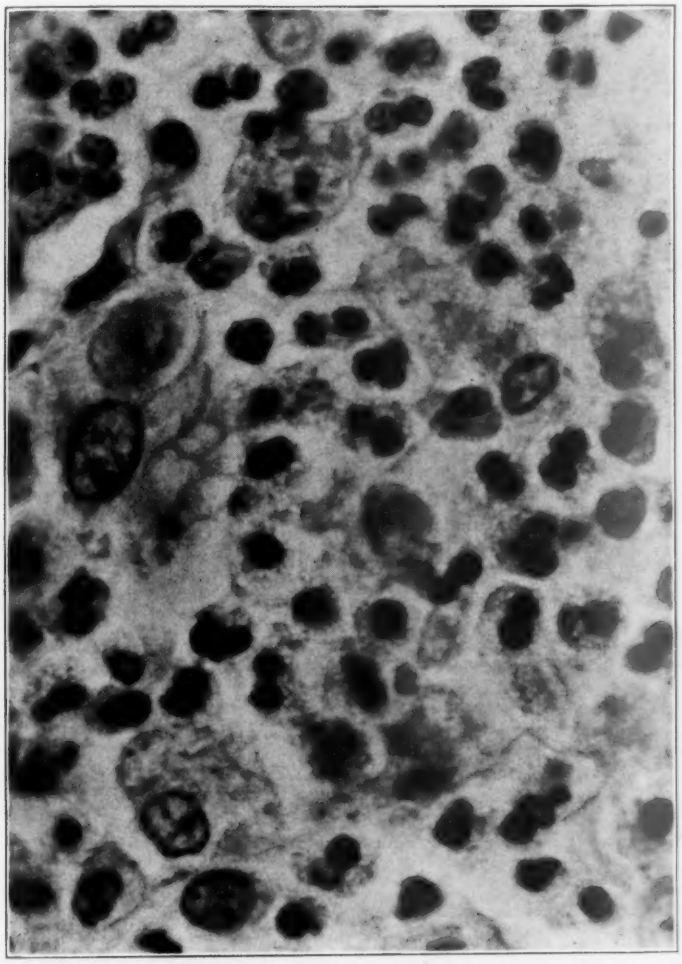

Fig. 3.—Biopsy of a nodule of the skull made in 1924 when the patient was 4 years of age. Note the absence of the usual foam cells and the marked infiltration of eosinophilic leukocytes (hematoxylin and eosin). The small cells with dense nuclei are eosinophils; the large cells, fibroblasts.

out," and there was no evidence of sclerosis of the surrounding bone. A lateral view of a midfrontal nodule suggested the absence of both skull tables. Roentgenograms of bones other than those of the skull and spine failed to show any unusual changes.

While the patient was under observation in the hospital the urination was frequent, but no record was made of the volume. Urinalysis showed no evidence of sugar or albumin, and the specific gravity was 1.016.

The white cell count was 9,200; the red count, 4,600,000. The reaction to the tuberculin test was positive at the end of twenty-four hours. Repeated Diazo tests gave negative reactions for Bence-Jones protein.

Tissue removed for examination from the midline frontal tumor was soft and light gray, and histologically showed a marked preponderance of eosinophilic leu-

Fig. 4.—The patient at 4 years, just before coming to the hospital.

kocytes (fig. 3). Atypical multiple myeloma was considered. Cultures of the tissue showed no growth.

After spending a portion of his stay on a Bradford frame the patient left the hospital nine weeks after admission feeling and looking well and showing considerable gain in weight. Pott's disease was thought to exist.

He returned to school within a month and played games like other children. Six months later a roentgenogram of the skull and spine showed less evidence of the lesions of the skull but an increased flattening of the tenth dorsal vertebral body. On Feb. 16, 1925, after a year's observation, additional roentgen ray examinations showed a complete absence of the "punched-out" areas in the skull. There had been no intervening therapy of any kind. There was still further flat-

tening of the tenth vertebral body, the cartilaginous plates apparently making contact throughout. The intercostal disks still appeared "clearcut" and of normal thickness.

The fourth roentgen ray examination (1928) failed to show any noticeable change except for the overgrowth of the anterior portion of the ninth and eleventh

Fig. 5.—The patient at 13 years, after enjoying good health for nine years. Note the absence of exophthalmos and marked kyphosis.

vertebral bodies, largely compensating for the almost completely destroyed tenth dorsal body. The last examination, made on Feb. 18, 1933, nine years after the first, still showed normal appearing skull tables (fig. 2 *C*) but increased thickness of the previously flattened vertebral body. Although the intervertebral disks above and below the thin body were intact, they did not have the thickness of the neighboring disks. The body itself appeared widened, and slight soft tissue densities

were seen at its lateral margins. The adjacent bodies showed a still further increase in their vertical thickness. There was no evidence of calcification or suggestion of a thick-walled abscess in this region.

At this time the boy was 13 years old, weighed 120 pounds (54.4 Kg.), was 5 feet 2 inches (157.48 cm.) tall, stood and walked erect, and gave a history of unimpaired health for more than eight years. The previous season he had been regular quarterback on the freshman high school football team. A photograph taken shortly before he entered the hospital in 1924 and one taken recently showed no external evidence of exophthalmos or deformity of the head. At the last examination the liver and spleen were not palpable; the urine was normal, and the cholesterol content of the blood was 150 mg. per hundred cubic centimeters of blood (within normal limits).

## COMMENT

Previous reported cases of xanthomatosis in which roentgenograms were made during life have shown defects in membranous bones, principally of the skull, only occasionally of the ribs, sternum, pelvis and long bones. None have shown involvement of a vertebral body accompanying the "punched-out" lesions of the skull producing the early symptoms and signs of Pott's disease, as in this case. Since the lesions of xanthomatosis are the hyperplastic reaction of the reticuloendothelial system resulting from the excess infiltration of lipoid in the body fluids, and since such an infiltration is found in bone marrow, as well as elsewhere, it should be expected that involvement of a vertebra would occur, at least occasionally. Without the presence of associated lesions of the skull a diagnosis of tuberculosis of the spine would most likely result. That lipoid deposits do occur in the vertebrae was demonstrated by Herzenberg's [6] patient in whom they were found at necropsy. In the case here reported the roentgen evidence was not that of the usual case of tuberculosis involving a vertebral body. Seldom, if ever, in tuberculosis is there complete gradual disappearance of the normal dense cancellous portion of a vertebral body with preservation of intact cartilaginous plates and intervertebral disks without sclerosis, débris or calcification as complete healing takes place. The rapid spontaneous remission and the lack of ankylosis, kyphosis or deformity without longer special treatment speak against the diagnosis of tuberculosis. This unusual phenomenon in which a vertebral body almost completely disappears, leaving the intervertebral disks intact, has been a more frequent finding in Gaucher's disease, but the associated changes in the long bones and other characteristic clinical evidence were not present in this case.

There remains little doubt that the multiple lesions of the skull which had largely disappeared within six months and completely within a year were not of an infectious or neoplastic nature. They simulated previously described proved cases of xanthomatosis. The absence of

6. Herzenberg, Helene: Die Skelettform der Niemann-Pickschen Krankheit, Virchows Arch. f. path. Anat. **269**:614, 1928.

foam cells in tissue removed from one of the soft areas in the skull is not surprising, as they have been conspicuously absent in the late stages of certain cases in which biopsies made early revealed their presence.[7] In this case the nodules were apparently in a late stage, as they were already disappearing at the patient's first visit; other members of the family had reported that three had disappeared. Those remaining were rapidly decreasing in size, as noted by palpation and roentgen observations.

The almost simultaneous appearance and disappearance of the lesions of the skull and spine supports a diagnosis of a single rather than of two distinct processes.

Pick[8] reported the finding at necropsy of clusters of Gaucher cells which had eroded the inner skull table, but "punched-out" areas in the skull have not been a frequent roentgen finding in either Gaucher's or Niemann-Pick's disease.

After reviewing the histologic material and the history submitted to him, Rowland expressed the following opinion:

> The clinical picture fits in with a type of bone xanthomatosis which, I believe, is as definite as Christian's syndrome. The pathologic specimen, while not positive for xanthomatosis, also could fit into the same picture. I have observed similar pictures in known xanthoma cases. As Dr. Jaffé has told you, the eosinophilia is striking. It seems to occur frequently in the chronic lesions of xanthomatosis.

The absence of exophthalmos, diabetes, discharging ears and other symptoms that have been frequently associated in other cases can best be explained by the harmless location of the nodules where symptoms would not likely be produced by the relatively small "punched-out" lesions of the skull. Their small size, likewise, was a favorable factor for early healing.

A return of the lesions seems most unlikely after nearly nine years of perfect health and development, but the patient will be watched for recurrences.

Sosman[9] demonstrated the advantages of local roentgen therapy for xanthomatic nodules, but the theory that the lesions may disappear rapidly and completely without roentgen or other special treatment and not recur for a long period seems supported by this case.

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7. Schulz, A.; Wermbter, F., and Puhl, H.: Eigentümliche granulomartige Systemerkrankung des hämatopoietischen Apparates (Hyperplasie des retikoendothelialen Apparates), Virchows Arch. f. path. Anat. **252**:519, 1924.

8. Pick, L.: Der Morbus Gaucher und die ihm ähnlichen Erkrankungen, Ergebn. d. inn. Med. u. Kinderh. **29**:519, 1926.

9. Sosman, M. C.: Xanthomatosis (Schüller's Disease; Christian's Syndrome): Report of Three Cases Treated with Roentgen Rays, Am. J. Roentgenol. **23**:581 (June) 1930; Xanthomatosis (Schüller-Christian's Disease, Lipoid Histiocytosis), J. A. M. A. **98**:110 (Jan. 9) 1932.

SUMMARY

A case presenting the clinical picture of xanthomatosis, as previously outlined by Rowland, is described. The patient came to the hospital because of acute pain in the back. A roentgenogram showed what seemed to be a compressed vertebral body. These findings led to an early diagnosis of Pott's disease. Many nodules on the head appeared on the roentgenogram as circumscribed areas of decreased density of the skull tables. The unusual histologic appearance of one of the nodules led to an interpretation favoring a myeloma. The child made a rapid and apparently complete recovery and has remained well since (nine years). In view of all the findings it was concluded that a diagnosis of xanthomatosis was more warranted than one favoring other forms of lipoid infiltrations, neoplasm or tuberculosis.

The main points of interest in this case are: (1) involvement of a vertebral body, successive roentgenograms and clinical observations taken over a long period suggesting the nature of the process; (2) the absence of characteristic foam cells in the tissue examined, and instead a manifestation of a late stage consisting of marked infiltration of eosinophilic leukocytes; (3) prompt and apparently complete recovery without roentgen ray or other special treatment.

# SEPTIC ENDOCARDITIS IN AN INFANT SEVEN WEEKS OF AGE

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BALTIMORE

Endocarditis in infancy is rare, but when it occurs it is more often associated with a septic than with a rheumatic process.[1] Many such involvements are not discovered until autopsy, because the heart frequently reveals no enlargement and no murmurs. When murmurs do occur, one's first thought is of congenital malformation of the heart. In the case reported here every one who listened to the heart commented on the fact that the murmur sounded more like that of an acquired lesion than like that of one of congenital origin; even so no one gave serious consideration to the possibility of infectious endocarditis.

## REPORT OF CASE

*History.*—H. J., a male Negro baby, aged 7 weeks, was admitted to the Harriet Lane Home on Dec. 18, 1931, because of labored and irregular breathing. The family history was essentially unimportant. The infant was born at full term and weighed 5 pounds (2,268 Gm.) at birth. He cried immediately. No snuffles, desquamation or difficulty in breathing were noted. The child was breast fed and gained well. There was no history of convulsions, attacks of cyanosis or illness of any sort.

One week before admission a mild cough developed. This did not disturb the infant greatly, nor was it sufficiently severe to keep him awake at night. The day before admission grunting respirations developed. That night the child seemed to breathe more quietly. Nevertheless, he continued to be fretful, and the following morning the respirations again became rapid and labored. That evening he seemed worse. He was brought to the hospital and was promptly admitted.

*Physical Examination.*—The temperature on admission was 37 C. (98.6 F.) and the weight 3,960 Gm. The general appearance was that of a well nourished colored infant with rapid, grunting Cheyne-Stokes respirations. There was definite retraction of the lower costal margins, but no dilatation of the alae nasi.

The head was normal, as were the eyes, ears, nose and throat. The lips were slightly bluish, but the gums were not particularly cyanotic. The chest was well formed.

The heart seemed slightly enlarged. The apex was just outside the midclavicular line. There was no shock or thrill. The heart sounds were very loud,

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From the Harriet Lane Home, Johns Hopkins Hospital.

1. White, P. D.: The Incidence of Endocarditis in Children, Am. J. Dis. Child. **32**:536 (Oct.) 1926.

especially at the apex and along the left sternal border, and the rate was very rapid—approximately 150 a minute. There was a harsh systolic murmur which was loudest at the apex, and was definitely transmitted to the axilla. It was also heard over the lower part of the sternum, but it was not audible over the base of the heart, beneath the clavicles or in the interscapular region.

The lungs were clear. The abdomen was soft. The liver was slightly enlarged, extending one fingerbreadth below the costal margin. The spleen also was enlarged and firm; the tip was palpable one and a half fingerbreadths below the costal margin. The genitalia were normal. The extremities were essentially normal. The reflexes were active and equal.

*Summary of Positive Findings.*—The patient was a well nourished infant with rapid, irregular grunting respirations and inspiratory retraction of the lower costal margins. The lips were slightly cyanotic. Slight enlargement of the heart was apparent, with loud heart sounds and a loud apical systolic murmur transmitted to the axilla. Both the liver and the spleen were enlarged.

The tentative diagnosis was: congenital malformation of the heart with moderate decompensation; congenital syphilis.

*Laboratory Data.*—Examination of the blood showed: red cells, 4,100,000 (the cells were of normal size and shape); hemoglobin, 70 per cent (Sahli), and the white cells, 13,000, of which 67 per cent were polymorphonuclear cells. The urine showed some evidence of congestion; occasional clumps of white blood cells and granular, hyaline and cellular casts were found on microscopic examination. The Wassermann reaction of the blood was negative. Roentgenograms showed the cardiac shadow extending 2.6 cm. to the right and 3.7 cm. to the left of the midsternal line; the aortic shadow measured 3.5 cm. The total transverse diameter of the chest was 11 cm.

*Course.*—The outstanding feature was the difficulty in respiration. There was a slight fever, from 37 to 38 C. (98.6 to 100.4 F.). On the second day after admission there was a severe attack of dyspnea. The respiratory rate rose to 70 a minute and the pulse rose to 158 a minute. The infant became cyanotic, and thick, tenacious mucus came from the mouth. Moist râles were heard at the bases of both lungs. The child's condition improved after the administration of 0.6 mg. of morphine, although he remained more dyspneic than formerly. The liver and spleen enlarged, each extending two fingerbreadths below the costal margin. The temperature rose abruptly from 37.4 C. (99.3 F.) at noon to 40 (104 F.) at 4 p. m., and dropped to 37.6 (99.6 F.) at 8 p. m.

The following day the infant was more dyspneic and apathetic. Although no thymus gland could be detected, it seemed possible that the respiratory difficulty might be due to thymic obstruction. Therefore the therapeutic test of one roentgen treatment was given but with no effect.

The patient died that night, obviously from cardiac failure.

*Report of Autopsy.*[2]—The heart showed some hypertrophy, but no Aschoff bodies and no scars. It weighed 35 Gm. It lay in the normal position, and the great vessels came off normally. The foramen ovale was about 4 mm. in width, but passed obliquely through the auricular septum, so that it was well covered by a curtain of tissue. There was a tiny blood cyst in the tricuspid valve near the line of closure. The pulmonary and aortic valves were normal. On the pos-

2. The pathology department of the Johns Hopkins Hospital prepared this report.

terior leaf of the mitral valve was a nodular mass about 1.5 cm. in the greatest diameter, suggesting a large vegetation. It was torn loose from the valve at one margin. The under surface of the valve was also rough and granular, and bits of tissue were friable. On picking up the valve the normal ridge formed by the line of closure appeared below the mass, and the chordae tendineae joined in the normal fashion. This thickened sheet of tissue was continuous with the wall of the auricle considerably above the point at which the valve ring was located, and there was a distinct recess apparently either in the myocardium or at the base of the ventricular wall, which formed a pouch with a granular lining behind the valve. Microscopic examination proved that this was an infection of the left ventricle just beneath the base of the mitral valve; part of the myocardium was destroyed, leaving a cavity with a ragged lining and a wall composed of fibrous tissue. The base of the valve was converted into a tense mass of connective tissue containing many wandering cells. The wall of the auricle appeared to be normal except at the point at which the valve was attached; at this point it was involved in the infection. In the fresher part of the vegetation bacterial stains revealed a fair number of gram-positive diplococci; a few of these organisms were definitely lancet-shaped, and it was thought that they probably represented pneumococci.

The origin of this lesion was not clear. It seemed possible that it began as an abscess in the ventricular musculature with an extension to the mitral valve, or the process may have gone the other way. The fact that the part most involved was toward the base of the valve was in favor of the former possibility. The portal of entry of the infecting organism was even more obscure. Evidence of previous pneumonia was sought as a source of the infection of the heart. Many of the alveolar walls appeared to be thickened with connective tissue, and were more cellular than normal, but nothing was found which could definitely establish the existence of organizing pneumonia. Stains failed to show any bacteria in the lungs.

The liver showed widespread midzonal necrosis. The spleen showed many foci in which the cells were clearly necrotic and breaking up, and the splenic pulp was filled with blood—this was apparently due to the necrosis. There were two small accessory spleens. The other organs showed nothing remarkable. The thymus and thyroid glands were normal. The gastro-intestinal tract revealed nothing unusual. The kidneys showed cloudy swelling. The suprarenal glands appeared to be normal. In the pancreas was a small localized hemorrhage on one side which appeared to be fresh. The pancreatic cells were filled with granular material; the islets were normal. The ribs showed a slightly irregular line of ossification, but there was nothing characteristic about this minimal irregularity.

The final diagnosis was: subacute myocarditis and mitral endocarditis (pneumococcal?); mitral insufficiency; chronic passive congestion of the lungs; slight lobular pneumonia; thickened alveolar septums; midzonal necrosis of the liver; necrosis of the spleen and hemorrhage into the splenic pulp, and accessory spleens.

## COMMENT

The heart showed an unusual and interesting picture, presenting a well recognized series of pathologic changes. There was a vegetation of the heart valve, with an abscess in the myocardium and bacteremia. The liver and spleen were both enlarged and scarred as a result of this process. The enlargement of the liver and spleen immediately suggested syphilis. When the Wassermann reaction of the blood proved to be

negative, the question was raised whether the enlargement of the liver was due to decompensation. Terminally this was true, but when first seen it was undoubtedly due to the chronic systemic infection.

Rheumatism seemed out of the question because of the age of the patient. My associates and I had thought of acute bacterial endocarditis as occurring only in the presence of some obvious disease. Chronic or subacute myocarditis or endocarditis at the age of 7 weeks without a history of a previous acute illness seemed highly improbable.

SUMMARY

A case is reported of a colored male infant, 7 weeks of age, who had a slightly enlarged heart with a loud apical systolic murmur transmitted to the axilla. In addition the liver and the spleen were both enlarged. Autopsy revealed a vegetation on the mitral valve causing mitral insufficiency and chronic inflammation of the liver and spleen.

# Progress in Pediatrics

## RELAPSING FEVER IN CHILDREN

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Hippocrates probably described the first epidemic of relapsing fever,[1] and no further mention of this disease was made until 1741, when Rutty[2] observed a disease of this type associated with typhus fever during an epidemic in Dublin. In 1857 Livingston reported that in South Africa a peculiar type of relapsing fever often followed the bite of a tick. During an epidemic in Germany in 1873, Obermeyer confirmed his earlier observation (1868) that relapsing fever was a spirochetosis by demonstrating spirochetes in the blood of a large number of patients. In 1904, the spirochete of African relapsing fever was discovered independently by a number of workers, and Dutton and Todd proved its transmission by a tick. In 1907 Novy discovered the spirochete causing the American disease. Sargent and Folley (1910) proved that European relapsing fever was transmitted by a louse.

The first case in the United States occurred in Philadelphia in 1844, and small epidemics of this disease which were thought to be importations from Ireland appeared in Philadelphia and New York during 1869. In 1874 Miller[3] described an epidemic among the Chinese population of Oroville, Calif., but these cases were frequently associated with typhus fever, and an absolute diagnosis could not be made.

With the exception of imported cases, relapsing fever was unknown in this country until Meader[4] in 1915 reported 5 cases from Bear Creek Canyon, Colo. Two years later Waring[5] reported a case in a 12 year old boy from the same focus. Briggs[6] described the first 2 cases of

1. Westbrook, F. F., in Allbutt's System of Medicine, London, The Macmillan Company, 1900, vol. 1, p. 140.

2. Rutty, quoted by Garrison, F. H.: History of Medicine, ed. 4, Philadelphia, W. B. Saunders Company, 1929, p. 706.

3. Miller, P. B. M.: Epidemic Relapsing Fever, Pacific M. & S. J. **8**:370, 1874-1875.

4. Meader, C. H.: Colorado Med. **12**:365, 1915.

5. Waring, J. J.: Relapsing Fever Endemic in Colorado, Am. J. M. Sc. **155**:819 (June) 1918.

6. Briggs, Le Roy H.: Relapsing Fever in California, J. A. M. A. **79**:941 (Sept. 16) 1922.

true relapsing fever arising in California in 1921. Weller and Graham [7] reported 5 cases from Texas in 1930.

### INCIDENCE

Louse-borne relapsing fever is endemic, but at times has been epidemic in Europe, Asia and Northern Africa. "Ten years ago there were hundreds of thousands—even millions of cases," each year, "while now there are only some scores of cases." [8] During the World War there were more than 12,000 cases in Serbia alone. Improvement in the social and sanitary conditions in these countries has reduced relapsing fever almost to a rarity except in Italy and Russia, where in spite of a marked decline it still persists in endemic form. Recent reports from China are lacking.

The chief focus of tick-borne relapsing fever is probably Central and South Africa. It is this type of the disease which occurs endemically in parts of Central and South America, Mexico and the United States and seldom becomes epidemic.

In the United States 6 cases have been reported from Bear Creek Canyon, Colo., and 5 from Texas, although in a recent article Graham [9] stated that there have been at least 40 other cases and that the disease is not nearly so rare in Texas as he first thought. Several cases have occurred in Nevada and Utah, and recently a case [10] was reported from Arizona. To date 38 cases have been reported in California.[11] Most of the cases have occurred during the summer, when the ticks are most active. In northern California, Polaris on the Truckee River, Packer Lake and Lake Tahoe are the chief foci of infection, while Big Bear Valley is the focus in southern California. Rapid transportation [12] by air of a person from an infected area has caused the sudden appearance of the disease thousands of miles from the source of infection.

Relapsing fever occurs less frequently in children than in adults, although the exact percentage is difficult to evaluate owing to the lack

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7. Weller, B., and Graham, G. M.: Relapsing Fever in Central Texas, J. A. M. A. **95**:1834 (Dec. 13) 1930.

8. League of Nations, Health Organization: Epidemiological Report, no. 12, December 1930, p. 481.

9. Graham, G. M.: Relapsing Fever Endemic in Texas: Possibility of Animal Reservoir, Texas State J. Med. **27**:226 (July) 1931.

10. Bannister, Kimball: Relapsing Fever, Southwestern Med. **14**:581 (Dec.) 1930.

11. Porter, Giles S., Director, California Department of Health: Personal communication to the author, April 10, 1933.

12. Fernan-Nunez, M.: Relapsing Fever: Its Occurrence in a Non Tropical Area, Wisconsin M. J. **30**:556 (July) 1931.

of details in the literature. According to Löwenthal [13] 83 per cent of the cases in a Moscow epidemic were in men, and Rabinowitsch stated that in Kiev men were infected 3.5 times more frequently than women and children. Levy [14] reported 360 cases in children from Odessa from 1917 to 1924; 120 cases occurred in children under 6 years, including 1 nursling, and 240 cases in children between the ages of 6 and 15 years. There was no significant sex incidence. Mackie [15] in a study of an epidemic in India found 170 boys infected, as compared with 114 girls. The boys were more heavily infested with body lice, which, according to Mackie, caused the difference in incidence. Of Pampana's [16] 92 cases in an epidemic in Colombia, South America, 14 occurred in children. Chu,[17] in a study of 26 epidemic cases in boys aged from 8 to 12 years, stated that in China infection is rare in children under 12 years of age. Scott [18] reported an interesting case in a 6 day old infant whose mother had her initial attack of relapsing fever during labor. Infection was thought to have taken place through the umbilical cord during delivery. Ten of the cases reported in California occurred in children.

## ETIOLOGY

Borrelia recurrentis is given various names, depending on the location from which it comes. Strong [19] has worked with many of the so-called species and has found but two, although more recent work has shown slight differences culturally and immunologically. According to Strong the difference is not great enough to warrant the division into species. Borrelia Novyi is the name given to the organism causing the North American disease.

Morphologically, the spirochete has an average length of between 15 and 26 microns, a width of 0.3 micron and usually from three to six turns which may not show up well on stained smears. In fresh preparations the organisms are very active, movement being in two directions, one of progression and the other of gyration. Multiplication [13] is by longitudinal and transverse fission.

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13. Löwenthal, quoted by Toyoda, H.: Relapsing Fever, Nat. M. J. China **17**:233 (April) 1931.

14. Levy, G. S.: Typhus Recurrens im Kindesalter, Ztschr. f. Kinderh. **42**:233, 1926.

15. Mackie, F. P.: The Part Played by Pediculus Corpusis in the Transmission of Relapsing Fever, Brit. M. J. **2**:1706, 1907.

16. Pampana, E. J.: Notes on Columbian Relapsing Fever, Tr. Roy. Soc. Trop. Med. & Hyg. **21**:315 (Jan.) 1928.

17. Chu, F. T.; Dietrich, Sarah, and Chung, S. F.: Relapsing Fever in Children: Study of 26 Epidemic Cases, Nat. M. J. China **17**:224 (April) 1931.

18. Scott, Annie, V.: Relapsing Fever: Case in Infant Aged 8 Days, Nat. M. J. China **17**:282 (Dec.) 1931.

19. Strong, Richard P.: Relapsing Fever, in Nelson Loose-Leaf Living Medicine, New York, Thomas Nelson & Sons, 1923, vol. 2, p. 337 B.

The spirochetes appear in the peripheral blood of monkeys and of certain rodents about two or three days after their entrance into the tissues. They divide rapidly and sometimes become more numerous than the red blood cells. Following this stage, which lasts from several hours to several days, they disappear from the blood until another period of rapid multiplication occurs. Usually, after several such attacks antibodies which destroy the spirochetes develop in the host.

There is evidence of a similar cycle in the louse and tick. After the vector has fed on an infected patient the spirochetes pass into the

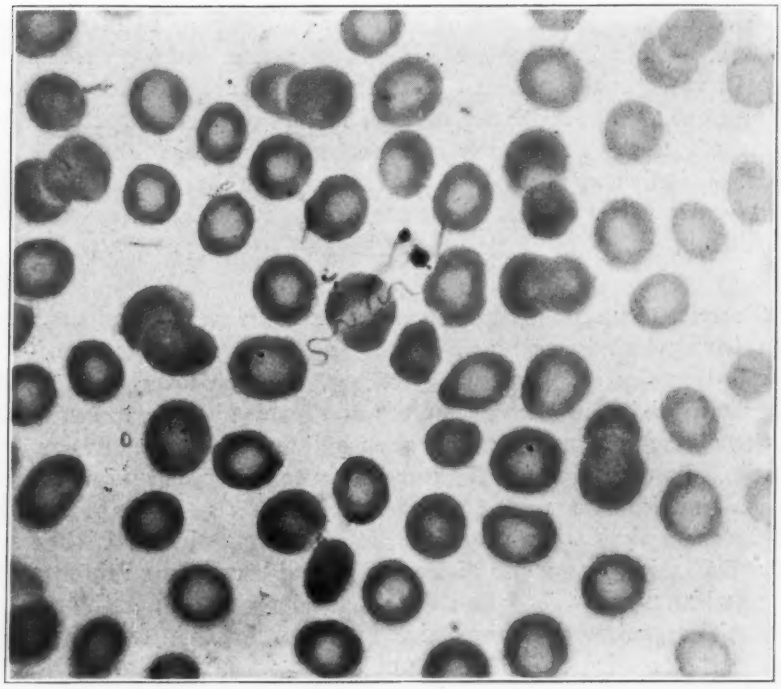

Fig. 1.—Parasite in a smear of peripheral blood.

alimentary canal where they rapidly disappear. About six or seven days later they may be found in the celomic cavity and body fluids and then in all the organs and tissues. Later the spirochetes disappear permanently. Leishman's [20] statement that the spirochetes undergo a metamorphosis into granules which under favorable conditions develop into spirochetes is supported by experimental evidence. It has also been

20. Leishman, W. B.: A Note on "Granule Clumps" found in Or. Moubata and Their Relation to the Spirochetes of African Relapsing Fever, Ann. Inst. Pasteur **32**:49, 1918.

demonstrated that once a tick is infected the infection may be passed on through the eggs for three generations; hence the egg, larval, nymphal and adult stages are all infectious.

### MODE OF TRANSMISSION

Relapsing fever is not usually transferred by the bite of a louse or tick, but more commonly by the vectors' being crushed on the skin

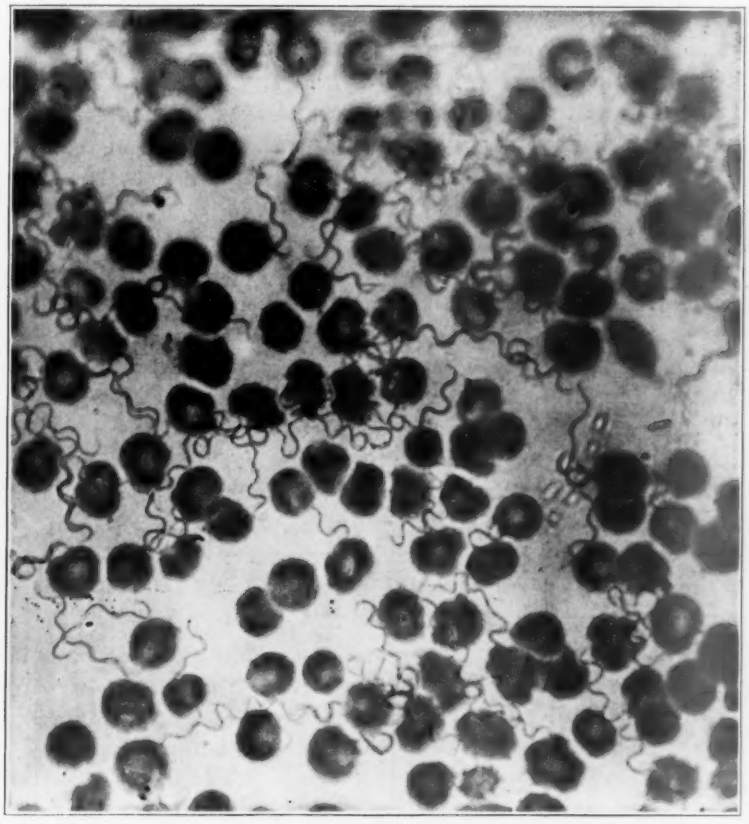

Fig. 2.—Parasite in a smear from an experimentally infected mouse, showing how the spirochetes multiply in this animal.

or by scratching an area where a tick has fed. According to Levy, the absence of scratching in the very young accounts for the rarity of the disease in this age group. However, some workers [21] believe that the spirochetes can pass through the unbroken skin. The organisms

21. Hendle, E.: A System of Bacteriology, by various authors, London, His Majesty's Stationery Office, 1931, vol. 8, p. 147.

are deposited on the host in the coxal fluid and feces. Nuttall [22] has transmitted Bor. recurrentis from mouse to mouse by means of crushed bedbugs. The bedbug, however, appears to play an unimportant rôle in the clinical transmission of relapsing fever. Biting flies and mosquitoes may carry the infection mechanically.

Weller and Graham were the first in this country to prove definitely that the tick is a source of infection. In their cases Ornithodorus turicata was the transmitting agent. During the summer of 1931 the California Public Health service found O. turicata in a cabin at Lake Tahoe, but the tick did not contain spirochetes.

The brilliant studies of Nicolle and Anderson [23] on relapsing fever in Tunis indicate that the spirochetes commenced as parasites of small mammals and that burrowing rodents serve as reservoirs of the disease. Similar conclusions were drawn by Clark, Dunn and Benavides in Panama, and Graham [7] recently indicated that the same facts are probably true in Texas. Porter, Beck, and Stevens [24] have found spirochetes in chipmunks and ground squirrels in California. As further evidence that rodents play a part in the epidemiology of relapsing fever, they relate the case of one of their field workers who seven days after accidentally smearing some blood from a rodent on his hands, on which there were several open lesions, became ill with relapsing fever.

Spirochetes may pass through the placenta in small numbers without pathologic changes occurring in the placenta. Some investigators [25] have found spirochetes in fetal mice while others have not. In the new-born infection takes place during birth. The disease runs a severe course if infection takes place early in pregnancy, and the fetus is found to be immune. Depending on the severity of the epidemic, abortions are more or less frequent.

Muhlens, Grothusen and others [25] have found that children and adults may act as carriers of relapsing fever. Spirochetes were found from fifty-four to ninety-eight days after the blood was found to be positive for the organisms. These patients were without symptoms.

### PATHOLOGIC CHANGES

Except for the possible presence of spirochetes in smears of the spleen, liver, brain and bone marrow, there are no characteristic post-

22. Nuttall, G. H. F.: On the Rôle of Insects, Arachnids, and Myriapods as Carriers in the Spread of Bacterial and Parasitic Diseases of Man and Animals, Johns Hopkins Hosp. Rep. **8**:1, 1899.

23. Nicolle, C., and Anderson, C.: On the Origin of Human Relapsing Fever, Bull. Inst. Pasteur **25**:657 (Aug.) 1927.

24. Porter, G. S.; Beck, M. Dorothy, and Stevens, T. M.: Relapsing Fever in California, Am. J. Pub. Health **22**:1136 (Nov.) 1932.

25. Ruge, Henry, in Mense, C.: Handbuch der Tropenkrankheiten, ed. 3, Leipzig, Johann Ambrosius Barth, 1929, pt. 1, p. 424.

mortem observations. The organs may show the evidence of toxemia and may or may not be stained with bile. The spleen is usually enlarged and sometimes shows infarction. Distention of the intestines and bladder has been found. Some particular organ may show a special complication.

### SYMPTOMS

The period of incubation is fairly well established for the disease as it occurs in California and Texas and varies between six and nine days.

Prodromal symptoms are uncommon, but in some cases there may be mental depression, languor, a chilly feeling and sweating. The attack is ushered in by a sudden seizure with a chill, and often in children by a convulsion. The chilliness may last for some time, and the temperature mounts rapidly. There is usually severe frontal headache. Nausea and vomiting are frequent, and the patient is usually compelled to go to bed. During an attack he may be shivering; the face may be flushed and the skin hot and dry, and he may appear toxic. A temperature of 104 F. and over is not uncommon, with the pulse rate correspondingly elevated. The eyes may show a mild conjunctivitis and jaundice. Nosebleed is rare. The tongue is usually coated; Levy believes that this is characteristic of the disease, as he found it in 91 per cent of his patients. Herpes is not uncommon with the first attack, and the mucous membrane of the mouth may show many white pinhead-sized papules. With the first attack there may also be a macular rash similar to rose spots over the abdomen and chest, which persists for from a few hours to days. Mild jaundice is a common finding in Europe and Africa but is rare in the cases occurring in California. Edema of the hands, face and feet is also rare.

Pulmonary signs such as cough and slight bronchitis may be encountered but are uncommon. In severe toxic cases signs of pneumonia may be elicited. The spleen is usually palpable, although it may not be with the first attack or perceptibly enlarged during the entire course of the disease. It was palpable in 80 per cent of Levy's cases, and Chu found enlarged spleens in 69 per cent of his patients. The liver may be slightly enlarged and tender. In severe toxic cases there may be abdominal distention and urinary retention, the bladder being distended as high as the umbilicus. Constipation is a common finding, although diarrhea may develop with or following an attack. Hemorrhages may occur. Convulsions [26] are said to be common in children, but they were observed in only 1 case in this series; however, nervous symptoms such

26. Manson, Philip H.: Tropical Diseases, London, Cassell & Co., Ltd., 1929.

as irritability, slight dulling of the mental processes and delirium are common.

The course of an attack may be marked by prolonged spells of shivering, excessive vomiting and subsequent thirst. Hiccup is occasionally seen. Rather severe pain in the muscles and joints of the thighs, shins and wrists, often the outstanding symptom, is not commonly noted in children, probably because they do not complain. A generalized burning is an occasional complaint.

Attacks usually last from two to seven days, although they may last only a few hours. Symptoms generally increase steadily to a crisis, though occasionally they decline gradually. The crisis is noted by a rapid fall in temperature, a decrease in pulse rate and profuse sweating.

Following an attack, except for weakness and occasionally nausea and vomiting, the patient is perfectly well and it is hard to convince him that he is still sick. The spleen usually decreases in size between attacks, only to become larger with each subsequent attack. After an interval of from two to eleven days subsequent attacks occur in untreated patients. These are usually less severe though an increase in severity may be seen. The number of relapses varies if the disease is untreated. One patient had three attacks, and an adult seen in consultation had eight; neither of these patients received specific treatment, and they had no further trouble.

The urine usually shows some albumin during an attack, but this is not significant. Casts are sometimes found, and white blood cells are rarely seen, though they have been found in considerable numbers.

A leukocytosis of from 12,000 to 15,000 with a predominance of neutrophils is a common observation during a paroxysm, although there may be a leukopenia. Lymphocytosis [27] may precede the appearance of the febrile stage by two or three days. An increase of basophils is sometimes found. Chu [17] reports that the platelet count was below 100,000 in 72 per cent of his cases and that the bleeding and clotting time were normal. A secondary anemia usually develops in untreated patients.

The Wassermann test [26] is strongly positive in 20 per cent of the cases in both the pyrexial and the apyrexial stage. Roaf [28] found it positive in 50 per cent of his cases.

The diagnosis is confirmed by finding the organisms in the blood. It is important that blood be taken during a paroxysm, as organisms are rarely found between attacks; however, in children they are not uncommonly found between attacks.[26] Fresh smears are best, as one is aided in the search for spirochetes by their motion and by that of the red blood cells. A dark-field apparatus is best, but it is not necessary.

27. Karwacki, L.: Leucocyte Count in Relapsing Fever, Presse méd. **33**:1138 (Aug. 26) 1925.

28. Roaf, H. E.: The Wassermann Reaction in Relapsing Fever, Brit. J. Exper. Path. **3**:59 (Feb.) 1922.

Direct smears, stained with Giemsa's or Wright's stain, are satisfactory, but the organisms may be difficult to find unless they are numerous. When the organisms are few, one will be aided by making a thick smear, laking the red blood cells with distilled water and then staining. Between attacks or when the spirochetes are too few to find by smear, the intraperitoneal injection of 1 or 2 cc. of the patient's blood into a mouse or rat, with later examination of the animal's blood, often proves of value. The animal's blood is usually found positive in from three to six days, but occasionally ten days are required before spirochetes are found. The injection of epinephrine [29] or of solution of pituitary into a patient suspected of having the disease is said to bring the organisms into the blood stream, making a diagnosis possible; however, this is of help only in the first infection.

### DIFFERENTIAL DIAGNOSIS AND PROGNOSIS

Malaria is the disease most often confused with relapsing fever. Typhus fever, with which it is frequently associated, typhoid and undulant fever may occasionally be mistaken for relapsing fever. In girls, a large amount of pus in the urine may make pyuria appear likely. The finding of the spirochete is essential for differentiation.

Relapsing fever is usually a self-limited disease, each relapse being less severe than the preceding one. In robust persons the disease is not especially dangerous, but in a weak or poorly nourished child it may be fatal. In Europe the mortality [8] is about 4 per cent, while in India, China and Africa it may be as high as from 30 to 50 per cent. Except for the questionable cases in Oroville in which the mortality was high, no fatalities have been reported in this country. Unfavorable signs are sudden syncope, acute cardiac dilatation, suppression of urine, convulsions, coma and severe toxemia. Relapses may occur from ten to twenty-one days after treatment.

### IMMUNITY

As a rule the spirochetes become fewer with each attack. The antibodies are extremely specific and are able to give complete protection only against the same race of spirochetes at the same stage of development; therefore, the antibodies produced after the first attack will not protect the body against spirochetes of the second attack until complete immunity is established.[21]

The importance of the reticulo-endothelial system in the development of protective substances has been clearly shown in the case of white mice infected with Bor. recurrentis. The mortality of normal mice was

29. Mishtchenko, I.: Diagnosis of Relapsing Fever and Malaria, Prophylak. med. **5**:20 (Feb.) 1926.

only 3.8 per cent; it was increased to 9 per cent in splenectomized mice in which the endothelial system had been blocked with colloidal iron.[30]

An uninterrupted attack confers a partial or complete immunity to reinfection with a spirochete of the same species, but is usually of short duration. Animals may be immune for several months. In man reinfection has occurred as early as in two months. In Africa children [31] are especially susceptible, while the older natives possess a partial or complete immunity.

## TREATMENT

Neoarsphenamine (or any of the arsphenamines) in one-half the usual recommended therapeutic dose is most effective when given intravenously at the beginning of a paroxysm. Albuminuria is not a contraindication to treatment. Relapses are common if the drug is given when the temperature is falling or between attacks, and giving the drug during the height of an attack is not without danger from the sudden liberation of endotoxins. Occasionally full therapeutic doses are necessary. Usually one adequate dose given at the proper time is sufficient, but the patient should be kept under observation for at least fourteen days.

## REPORT OF CASES

The following case has previously been reported in detail.[32]

CASE 1.—J. B., a boy aged 5½ years, had a normal family history except for a possible contact with tuberculosis in the father.

*Present Illness.*—The boy had been in Big Bear Valley for about two weeks when, on June 6, 1931, he had a temperature of 106 F., two convulsions, vomiting and occasional delirium; the attack lasted twenty-two hours. The physical examination showed no abnormalities except moderate dehydration and evidence of toxemia. The following day he had a crisis, but previous to this abdominal distention and urinary retention were noted. The bladder could be palpated as high as the umbilicus. Examination of the blood revealed a leukocytosis of 16,850 with 91 per cent polymorphonuclears; a smear was negative. A few pus cells and some albumin were found in a catheterized specimen of urine. A second attack three days later was less severe and lasted only eighteen hours. The spleen was palpable for the first time. There were 4,600 white blood cells, 54 per cent of which were polymorphonuclears, and the smears were still negative. The Widal test, the tuberculin reaction and blood cultures were all negative. Relapsing fever was considered. Six days later he had a third attack which lasted sixteen hours, but the smears were still negative. The following day while the patient was afebrile one spirochete was found, but the observation could not be confirmed. The disease seemed to have run its course when four days later he had a fourth attack

30. Kritschewski, J. L., and Rubenstein, P. L.: Ztschr. f. Immunitätsforsch. u. exper. Therap. **51**:27, 1927.

31. Stitt, E. R.: The Diagnosis and Treatment of Tropical Diseases, ed. 2, Philadelphia, P. Blakiston's Son & Co., 1907.

32. Varden, A. E.: Relapsing Fever; Report of a Case, California & West. Med. **36**:344 (May) 1932.

lasting twelve hours. At that time fresh and stained smears were positive for spirochetes of relapsing fever. He was treated with 0.15 Gm. of neoarsphenamine, and the temperature fell with a sharp reaction twenty-four hours later. When the temperature started to rise again five days later, another spirochete was found. Neoarsphenamine was given at that time and again four days later. His course thereafter was uneventful.

CASE 2.—C. A. was a girl, aged 5 years, whose family arrived in Big Bear Valley on June 28, 1931. A few days later the father noted that the child had a few insect bites which he considered were from a mosquito. On July 9 she had chills and fever. This attack lasted four days with a variation in temperature from 100 to 105 F. On July 10 a tick was found in her bed but got away. During the attack she complained of headache and "stomach ache" and was toxic. She had had three attacks of cystitis some months previously, and as considerable pus was found in her urine at this time, she was treated for pyuria.

The patient was first seen on July 12 at about the end of her crisis. The results of the physical examination were negative except for a barely palpable spleen. The cell count showed 8,100 white cells with 74 per cent polymorphonuclears, but no spirochetes were found in the smear. There was a trace of albumin in the urine and from 35 to 50 white blood cells per high power field. The urine was practically the same the following morning except for a few red blood cells. She was discharged as recovered, and the father was instructed to have smears made if the fever recurred. She returned to Big Bear Valley and on July 17 complained of headache; the following day she had a second attack. Her temperature varied between 100 and 105 F. during this attack. Unfortunately no smears were taken. Pus was again found in the urine. On July 21 she vomited persistently and had a severe nosebleed; her grandfather reported that she screamed and complained of pain as if she had a stone somewhere in the urinary tract.

She was seen the second time on July 22 at about the end of a crisis. She was pale, and the spleen was definitely larger than on the first examination. The white cell count was 12,000 with 72 per cent polymorphonuclears, but the smear was negative for spirochetes. The urinalysis showed from 12 to 15 white blood cells per high power field. Roentgen examination of the kidney, ureter and bladder gave negative results. She was referred to a urologist who advised a genito-urinary study.

A third attack in Santa Barbara on August 5 was accompanied by a temperature of 104.5 F. The cell count showed 50 per cent hemoglobin and 3,500,000 red cells. Smears made at this time were positive for spirochetes, and the child was given 0.15 Gm. of neoarsphenamine that evening, with a rather severe reaction.

CASE 3 (case of Dr. Clain F. Gelston and Dr. Emmett E. Sappington of San Francisco).—M. L., aged 12 years, was a resident of Los Angeles. The past history and family history were irrevelant.

*Present Illness.*—On July 10, 1931, the child arrived at Brockway, Lake Tahoe, for a vacation. During the first week she was bitten several times by what, from the description, appeared to be ticks. On July 16 there was a sudden acute onset of fever (104 F.), headache, prostration, nausea, pallor, a stiff neck, a positive Kernig sign and slight tenderness in the lower left quadrant of the abdomen. The spleen was not palpated. The temperature fluctuated for three days and then dropped to normal. Except for some evidence of fatigue, the child was well for five days. On July 26 there was a relapse with a temperature of 104 F., prostration, drowsiness, very slight headache and some subcyanosis.

The child was brought to San Francisco, arriving on July 26, and placed in the Dante Sanitarium. Except for the observations noted, the general physical condition was normal. Roentgenograms of the sinuses and chest were negative. The Widal test, cultures of the blood and stool and urinalysis gave negative results. The blood count was normal except for the presence in the smear of an unusual number of lymphoblastic cells, such as are encountered in leukemia. A careful search on July 29 demonstrated the spirochetes of relapsing fever.

The course in the hospital showed a temperature of 104.3 F. on the day of entry and of 103.8 F. the next day. The following two days the temperature remained normal. On August 1, the next day, the maximum temperature was 102.8 F. On that day 0.3 Gm. of neoarsphenamine was given intravenously. The temperature dropped to normal the following day and remained so until the date of discharge, August 6.

Case 4 (case of Dr. William Palmer Lucas, San Francisco).—R. D., a boy aged 8 years, entered the University of California Hospital on Aug. 24, 1931. The chief complaint was attacks of fever for two years. The family and past histories were unimportant. Since the summer of 1929 he had had attacks characterized by high fever, headache, nausea and vomiting associated with infection of the upper respiratory tract. These attacks usually lasted from two to five days, and the fever was usually out of proportion to the infection. For the past six weeks the attacks had been different. On July 13, 1931, while at Lake Tahoe, he experienced a chill; the temperature rapidly rose to 106 F.; he vomited, complained of pain in his legs and became prostrated and delirious. The physician who was called noted stiffness of the neck. The attack lasted thirty-six hours; following it he seemed well and ready to play. Eleven days later he had a similar attack, but his temperature was only 102 F. Seventeen days later he had a third attack with a temperature of 103 F.

On admission the results of physical examination were negative except for evidence of recent nosebleed and a palpable liver and spleen.

The observations on the blood were as follows: hemoglobin, 86 per cent (Sahli); red cells, 4,370,000; white cells, 5,240; polymorphonuclears, 34 per cent; eosinophils, 1 per cent; basophils, 1 per cent; large lymphocytes, 23 per cent; small lymphocytes, 35 per cent. Repeated examinations for spirochetes gave negative results. Urinalysis, the tuberculin test and blood serum agglutination tests gave negative results.

During his four days in the hospital he had no fever and appeared so well that he was discharged with instructions to return immediately on any rise in temperature.

He was readmitted on September 1, having complained of pain over the right tibia the day before. He also complained of anorexia. The parents recalled that he had an insect bite on the foot while at Lake Tahoe. At the time they thought this to be from an ant. The physical examination showed the same results as on his first entry except for some tenderness over the lower third of the right tibia. Roentgenograms of the legs showed nothing abnormal.

The temperature was normal on admission but rose to 38.2 C. (100.76 F.) that evening, and the pain became so severe that codeine was necessary for comfort. With the rise in temperature a systolic murmur was noted at the cardiac apex. It was not transmitted. In twelve hours the temperature was normal. The following day he again complained of pain over the tibia and at 11 p. m. his temperature was 39.5 C. (103.1 F). The white cell count was 11,100 with 83 per cent poly-

morphonuclears, and the blood smears were positive for spirochetes. He was given 0.2 Gm. of neoarsphenamine the following day, after which he made an uneventful recovery.

CASE 5 (case of Dr. Robertson Ward, San Francisco).—L. C., a boy, aged 12 years, was spending the summer at Lake Tahoe near Calneva Lodge. About Aug. 1, 1931, he became ill with a fever (from 102 to 103 F.), headache, slight nausea, loss of appetite and general malaise. He was ill for three days; then his temperature dropped suddenly, and he felt fairly well until August 11, when he had a similar but less severe attack. On August 19 he had a third mild attack lasting only two days. Smears taken at this time were positive for spirochetes. There was no history of bites. No specific treatment was given, and he had no further relapses. The spleen was not palpable at any time.

CASE 6 (case of Dr. Newell Jones of Hollywood, Calif.).—P. H., a boy aged 9 years, had been at a camp at Big Bear for about a month when he was suddenly taken ill with a high temperature, extreme headache and some abdominal pain. That is all that could be determined about his first illness, as neither his mother nor any one else had talked directly with those in charge of the camp, and we had only the boy's story. In three or four days he was well, but was sent home.

Five days after the remission of the fever from the first spell, his temperature again suddenly rose, with headache, abdominal pain and one spell of vomiting. He was extremely drowsy and talked a little irrationally on wakening, but this was the only sign of delirium or nervous symptoms.

About 10 o'clock on the night of August 22, which was about five days after the remission, he began complaining of headache and was a little delirious. The next day he was seen between 4 and 5 o'clock in the afternoon with a temperature of 104.5 F., a pulse rate of 130, a normal respiratory rate, a complaint of headache and abdominal pain and a marked aversion to having anything done. He complained of pain when the abdomen was examined, but there was no rigidity or tenderness. The results of the physical examination were entirely negative. In conversation he gave somewhat rambling answers.

Blood taken at this time showed 12,000 white cells, with 69 per cent neutrophils, and was positive for spirochetes.

He was given 0.30 Gm. of sulpharsphenamine intravenously. His temperature was normal in twenty-four hours, and he has not had a relapse since.

During the summer of 1932, 4 cases of relapsing fever in children were seen in consultation with Dr. Godfrey, San Bernardino County Health Officer, and Dr. Williams of Big Bear Valley. These cases were in transients, and hence complete records are lacking. They were similar to the cases reported. Enlargement of the spleen was noted on palpation in 2 of the 4 cases.

## COMMENT

Symptomatically relapsing fever as it occurs in California resembles the African form of the disease. The symptoms are much more violent than those of the European form, for in Europe the disease is mild unless complicated by typhus fever, which accounts for its high mortality in that area. In Africa the mortality is high probably because of complications and because the victims there are usually in poor health, while in California, even though the disease is usually fulminating, it is gener-

ally uncomplicated and its victims are persons in general good health. Prompt treatment is also a factor in the low mortality in California.

According to Toyoda, there is a bacteriologic relation between the European and the American type and there is also a relation between the European and the African, but none between the American and the African variety. The European type is between the other two.

## SUMMARY

1. A short review of relapsing fever is presented.

2. Ten cases of relapsing fever in children are reported.

3. A brief comparison between the American, European and African forms is given.

Medico-Dental Building.

# ACUTE ASPHYXIA FROM INTRABRONCHIAL RUPTURE OF A TUBERCULOUS MEDIASTINAL GLAND WITH RECOVERY

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NEW YORK

The sudden rupture of a tuberculous tracheobronchial lymph node with discharge of its contents into the main air passages is usually followed by death from asphyxia. Of ninety-four cases * described in the literature in sufficient detail to permit inclusion in this study, only nineteen ended in recovery. I wish to present another case, the first to be reported from this country. A tabular survey is given of the cases in which the patient recovered from the asphyxial episode. A complete bibliography of all proved cases showing the acute phase of this clinical entity is added.

## REPORT OF A CASE

*History.*—H. C., a boy of 16 months, was admitted to the Babies' Hospital on Jan. 24, 1932, because of nasal discharge of ten days' duration and noisy respiration for seven days.

The father was living and well; the mother was reported to have hypertension. A brother, 16 years of age, had had a cough for six weeks, which had recently been accompanied by night sweats; he had not been shown to have pulmonary tuberculosis but had not gained weight lately and tired easily. A sister, 12 years of age, was well. Two other sisters, 9 and 4 years of age, respectively, gave positive reactions to tuberculin tests and showed enlarged mediastinal shadows on roentgen examination. A brother died in December 1929 (before the patient was born) of tuberculous pneumonia and miliary tuberculosis, proved at autopsy. The patient was the sixth child. Two maternal uncles and one maternal aunt died of tuberculosis in 1916, 1926 and 1928, respectively.

The patient was born by normal delivery, weighing 10 pounds (4,550 Gm.) at birth. No cyanosis or rash was noted. He was breast fed for two months and

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The case was reported at a meeting of the Section of Pediatrics of the New York Academy of Medicine, May 11, 1933.

From the Babies' Hospital and the Department of Pediatrics, College of Physicians and Surgeons, Columbia University.

* Over thirty probable cases have been omitted because of inadequate description. It is reasonable to infer that, owing to the greater interest accompanying recovery and the consequent keener incentive to put such cases on record, the incidence of fatalities is higher than one might deduce from published observations, and the ratio of deaths to recoveries likewise greater.

then given cow's milk formulas. Vitamins were administered regularly and in sufficient amounts. He sat up at 5 or 6 months, walked at about 11 months and cut his first tooth at 12 months of age; he had not commenced to talk before admission to the hospital.

He was apparently well until six months before admission, when he had "pneumonia" which lasted three or four weeks; for at least a week he had a temperature of from 103 to 104 F. Later he had chronic bronchitis and was followed in a clinic. A tuberculin test was not made.

For ten days before admission he had had a cold, with nasal discharge. Seven days before admission his breathing became noisy during excitement or crying. At such times stridor was present during both phases of respiration. He had coughed little and had not vomited. His appetite remained good, he was playful and happy, and there was no fever. He was seen twice by a physician, who after the second visit referred him to the hospital because he was not improving. No cyanotic or severe dyspneic attacks had been noted, and there was no history of aspiration of a foreign body.

*Examination.*—The child was well developed and nourished and did not appear ill. His temperature on admission was 100.2 F. His physical measurements were essentially normal, and his weight was 22.6 pounds (10,300 Gm.). He cried when disturbed and during crying showed moderate cyanosis, a marked expiratory stridor and a less marked inspiratory crow, the latter accompanied by noticeable substernal and subcostal retraction. His breathing was improved by hyperextending the neck. The voice remained clear and free from hoarseness. The anterior fontanel was open, measuring 3 by 4 cm.; craniotabes was not present. There was a purulent discharge in both nares. The tonsils were moderately enlarged and distinctly red, and the entire pharynx was injected. Digital as well as visual exploration of the pharynx failed to discover retropharyngeal or peritonsillar swelling. Laryngoscopy showed an edematous epiglottis; both aryepiglottic folds were greatly swollen, bulging into the larynx. No membrane, exudate or foreign body was seen. The ear drums were normal. The chest was symmetrical, and the two sides expanded equally. Percussion showed normal resonance on both sides. Breath sounds were everywhere harsh and stridulant, expiration was prolonged and rhonchi were heard on both sides. The symmetrical character of the signs suggested that whatever respiratory obstruction was present was located above the tracheal bifurcation. The heart was normal. The spleen was palpable just below the costal margin. Both lower extremities showed slightly enlarged epiphyses and reduplication of the internal malleoli. There were palpable cervical and inguinal glands, the largest being the size of a pea. Neurologic examination gave negative results. The impression on admission was: acute laryngitis; acute pharyngitis and tonsillitis, and rickets.

*Course.*—The patient was placed in a croup tent and given atropine and barbital for symptomatic relief. He passed a restful night and was comfortable in the morning. A throat culture for Klebs-Loeffler bacilli gave negative results; examination of the blood revealed 5,200,000 erythrocytes per cubic millimeter and 12.7 Gm. of hemoglobin per hundred cubic centimeters (75 per cent on the Sahli scale); there were 12,200 leukocytes, of which 67 per cent were polymorphonuclears and 33 per cent, lymphocytes. The urine was normal. A tuberculin test (0.1 mg. of old tuberculin intracutaneously) after forty-eight hours showed an area 2.5 by 2 cm. of erythema and an area 0.8 by 0.8 cm. of induration. A roentgenogram of the chest taken on the morning after admission (fig. 1) showed a spherical shadow located in the right supracardiac region and encroaching on the lumen of the

trachea, which was in the midline. The consensus was that the shadow was due to enlarged peribronchial glands. There was partial atelectasis of the middle lobe of the right lung, which was clearly outlined by the thickened interlobar pleura. Some mottling was seen in the upper part of the lower lobe of the right lung, suggestive of a pneumonic process in that region. The Kahn test of the blood was negative.

During the first few days the patient's temperature was normal, and his condition improved until the morning of the fourth day after admission, when he was suddenly seen to fall from a standing position, striking his head on the side of the crib. On examination, he was found to be markedly cyanotic; there was great

Fig. 1.—Roentgenogram of the chest taken on Jan. 25, 1932, the morning after admission. There is a dense shadow in the right supracardiac region, spherical and encroaching on the lumen of the trachea, which, however, is in the midline. Extending obliquely downward and outward from the right hilus and reaching the lateral thoracic wall at the level of the ninth rib, the thickened interlobar pleura can be followed, outlining a partial atelectasis of the middle lobe of the right lung. Some mottling can be seen in the upper part of the lower lobe of the right lung, suggestive of a pneumonic process. The left pulmonary field is essentially clear.

dyspnea, with intercostal retraction, and auscultation indicated that he was getting little air into his lungs. Laryngoscopy was attempted but not completed because the child stopped breathing and became more cyanotic. Passing an O'Dwyer tube did not bring relief, and respiration was not resumed until the tube was withdrawn. On removal the tube was found to be plugged with thick, viscid material. Tracheotomy was performed immediately, and a 2 year tube inserted; no improvement was

noted. Vigorous suction, applied by a soft catheter passed through the tracheotomy tube, resulted in the removal of much thick, caseous material. Respiration thereupon became easy, and the child was thoroughly relieved. By suction, which it was necessary to apply frequently, large amounts of caseous material were removed during the course of the day, the largest single piece recovered measuring 4 by 2 by 2 mm. Microscopic examination showed it to consist of caseous débris containing many acid-fast bacilli. Laryngoscopy performed after the tracheotomy tube had been inserted showed a normal larynx. Following this examination, twitching of the hands and mouth was noted for a few minutes.

For several days following tracheotomy, there was marked symptomatic improvement, though the patient remained fretful and his cough sounded somewhat croupy. The temperature was normal. On the seventh postoperative day a smaller tube

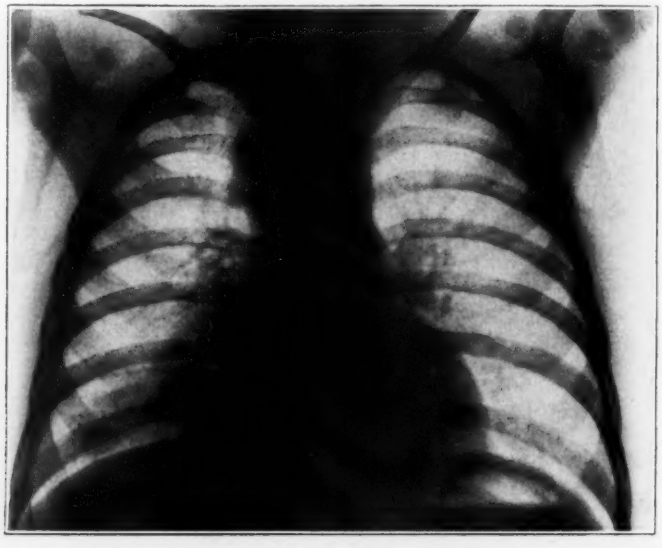

Fig. 2.—Roentgenogram of the chest taken on February 8, fourteen days after the taking of the first plate (fig. 1) and three days after the first removal of the tracheotomy tube. Compared with the preceding film, it shows an increase in the lung markings in the right middle and lower lobes. The interlobar fissure remains visible. The paratracheal shadows show practically no change in contour.

was inserted without causing dyspnea. On the following day (eighth) the tube was removed. A roentgenogram (fig. 2) taken on the eleventh day showed no change in the spherical hilus shadow; the lung markings in the right lower field were intensified, and the interlobar fissure was still visible. Laryngoscopy showed no abnormality. On the eighteenth postoperative day, while eating breakfast, the patient suddenly became cyanotic, perspired profusely and exhibited dyspnea accompanied by marked expiratory stridor. No treatment was instituted, and the patient gradually became more comfortable, so that at the end of three hours cyanosis had disappeared and dyspnea and stridor were less pronounced. The following day bronchoscopy, performed by Dr. Kernan, disclosed a profuse discharge of pus from both bronchi. The mucous membranes of the trachea and bronchi were intensely congested. Much granulation tissue was found at the site of the trache-

otomy wound, which bled freely when touched. It was considered possible that caseous particles might collect at the granulation site and cause dyspneic attacks. The exact source of the discharge could not be determined at this time. After the bronchoscopy there was a great increase in expectoration; the temperature continued to be normal, as before.

Two days later (twenty-first postoperative day) the patient had marked expiratory stridor, with slight stridor during the inspiratory phase. Between 3 and 6 p. m. he had two attacks marked by apprehension, severe dyspnea and cyanosis. In order to forestall the possibility of fatal asphyxia during one of these attacks, it was decided to repeat the tracheotomy. This was accomplished satisfactorily, although with great difficulty, chiefly because of distortion from the healing of the first wound and in spite of the fact that the opening into the trachea made three weeks previously had not entirely healed. The next four days were uneventful. Suddenly, at 8 a. m., on the twenty-sixth day after the first operation, the patient stopped breathing and became deeply cyanosed. He was relieved by removing the inner tracheotomy tube temporarily and applying suction through the other tube. At 5 p. m. of the same day he had another cyanotic attack associated with restlessness and a small volume of tidal air. A catheter inserted 2.5 cm. into the tracheotomy tube met definite resistance. After a few applications of suction, a caseous mass the size of a small bean was recovered, whereupon the symptoms of respiratory obstruction were instantly relieved. Microscopic examination of the piece removed showed tubercle bacilli. From this day on the patient's course was chiefly uneventful. Examination of the chest at frequent intervals from the end of this acute asphyxial stage until the day of discharge failed to reveal any physical signs of an active tuberculous process.

On the forty-seventh day after the first tracheotomy, bronchoscopy was again performed. The condition was found to be much improved: There was less granulation around the tracheotomy wound, and the mucous membranes were only slightly congested. Excessive granulations on the medial side of the right bronchus, close to its origin at the bifurcation, were thought to indicate the site of perforation, now in a state of healing. Following bronchoscopy there was a great increase in thick discharge through the tracheotomy tube; suction was used every two hours for three days. The patient's temperature remained normal. Examination of the blood at this time showed 5,100,000 erythrocytes per cubic millimeter and 14.4 Gm. of hemoglobin per hundred cubic centimeters (85 per cent on the Sahli scale); there were 11,800 leukocytes, of which 60 per cent were polymorphonuclears, 27 per cent lymphocytes, 5 per cent large mononuclears, 5 per cent eosinophils, 1 per cent basophils, 1 per cent myeloblasts and 1 per cent myelocytes.

The inner tube was changed almost daily; the patient was up and about and free from symptoms. On the eighty-third postoperative day there was a single brief cyanotic spell. For several days previously the discharge of mucus from the tube had been excessive. It is interesting to note that tubercle bacilli were again recovered from the discharge, nearly three months after the original perforation. One week later, laryngoscopy was performed. The larynx appeared normal, and it was considered time to begin plugging the tube partially. The following week the amount of discharge had again increased, and the closing of the tube was delayed for one reason or another until one hundred and eighteen days after the first tracheotomy. Then, for the first time in two months, there was some difficulty in replacing the tube. It was left out for three minutes without embarrassing the patient. No tubercle bacilli were found in the discharge at this time. Two days

later the tube was permanently removed. The patient breathed well both in the erect position and when sleeping, and there was no inspiratory retraction. It is interesting that for a week following removal of the tube there were daily fluctuations in rectal temperature between 97 and 99.6 F.

He was kept under close observation for the next month and, except for a common cold of a few days' duration, continued to improve. He was discharged to his home on June 23, 1932, after a hospitalization of five months (one hundred and fifty-two days). His condition was excellent.

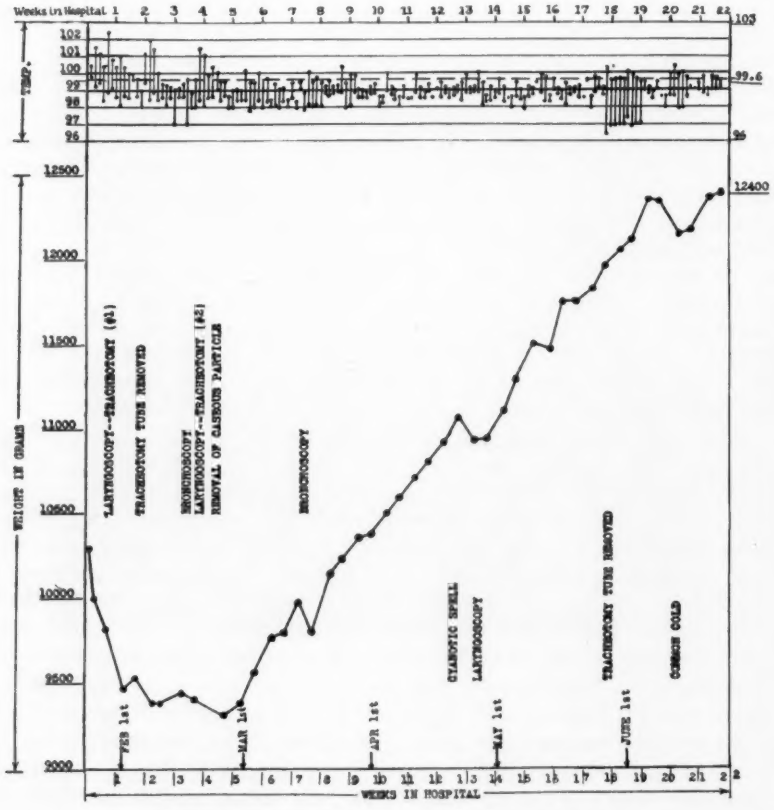


Fig. 3.—The lower portion of the chart shows the weight in grams (heavy continuous line) plotted against the weeks in the hospital. The vertical lines in the upper portion show the daily excursion of rectal temperature (the horizontal dotted lines represent 99.6 F.). Operative procedures and salient points are mentioned.

During the first month in the hospital, when the patient's illness was relatively acute, he lost 2.2 pounds (980 Gm.). Throughout the last four months he gained regularly, the total increment during the period being 6.75 pounds (3,080 Gm.), representing an average gain of 25 Gm. per day (fig. 3). He was given the routine hospital diet for well children, with adequate vitamins, and also daily exposure to a General Electric sun lamp. During the first month fever was noted for about

two weeks; this bore a definite relationship to the operative procedures. His temperature curve was normal throughout the last four of the five months of hospitalization.

During the summer months, under relatively unfavorable conditions at home, he lost about ½ pound (220 Gm.). Physical examination on September 8, two and one-half months after discharge, showed a well developed and nourished, healthy-appearing boy. No abnormal physical signs could be detected in the chest. The spleen was palpable just below the costal margin. A roentgenogram of the chest showed that the enlarged mediastinal shadow had disappeared.

The patient remained well until March 1933, when he contracted measles from a sister. The illness was not prolonged, and the cough was not distressing. Roentgen examination ten months after discharge (fig. 4) showed no widening of the

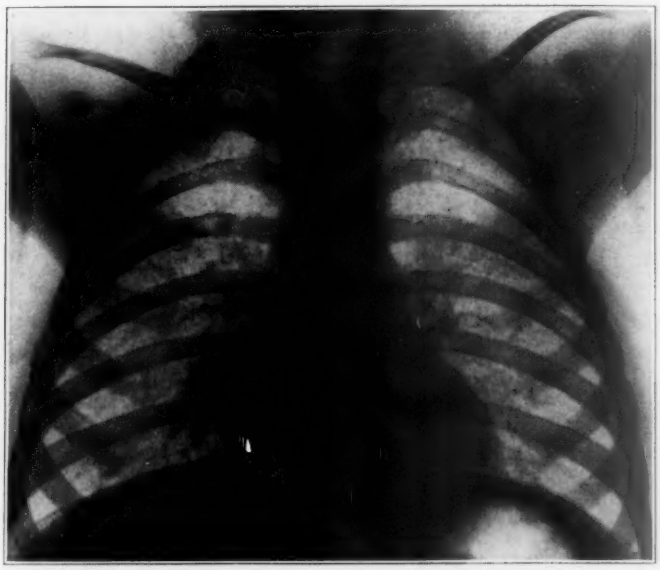

Fig. 4.—Roentgenogram of the chest taken on April 20, fifteen months following the rupture. There is no widening of the mediastinal shadow. In the right midclavicular line, just above the diaphragm, there is a crescent-shaped shadow approaching the density of calcium which is believed to be the primary focus. The pulmonary fields show no areas of mottling.

mediastinal shadow; calcification of the apparent primary focus was noted in the midclavicular line on the right side just above the diaphragm. The patient was symptom-free at the time.

He has continued to do well, and at the time of writing, thirteen months after discharge from the hospital (one and a half years after the perforation), his general condition is excellent. In his first year since discharge he has gained 6.5 pounds (3,000 Gm.), a total gain of 13.25 pounds (6,080 Gm.) during the 16 months following the termination of the acute episodes. It has proved impossible to convince his parents that he might need a special regimen at home. He has been so active, and his disposition so amiable, that they have subjected him to the same irregular hours for meals and rest that they observed with their other children.

It must be admitted that he has thrived in a manner that could scarcely be improved on. Except for chronically enlarged tonsils and adenoids and a well healed tracheotomy wound his physical examination reveals nothing remarkable.

COMMENT

Bronchogenic spread of pulmonary tuberculosis following the perforation of tuberculous mediastinal glands into the main air passages with a fatal ending is a familiar process, but obstruction to breathing as a result of the sudden rupture of a gland into the trachea or large bronchi is rarely seen. Nevertheless, the picture probably presents itself more often than it is recognized, and reports in the literature may be considered to cover only a small fraction of the cases actually observed either during life or at the autopsy table. If the content of the gland or glands is in a liquid state at the time of rupture, the material may be expectorated without causing an asphyxial episode. However, if the material has a semisolid consistency, a portion of it may plug the tracheal lumen or glottis entirely and cause sudden death.

Most of the reports of this clinical entity are to be found in the French and German literature, with a smaller number in Italian and other periodicals. Schmiegelow,[77] in 1918, discussed the cases published in the Scandinavian literature up to that time. A number of case reports were given in the proceedings of the meetings of the Pathological Society of London in the latter half of the nineteenth century, and several brief pathologic reports without discussion appeared in the proceedings of the New York Pathological Society about 1900. At one of these meetings the autopsy observations in two cases were mentioned. Many textbooks of pediatrics and tuberculosis make some reference to the subject. Chevalier Jackson,[107] discussing bronchoscopic findings in tuberculosis of the tracheobronchial tree, stated: "In a number of instances, the entire lumen of the bronchus was occluded by cheesy débris of a peribronchial gland which had eroded through." The bibliography which I have compiled gives a picture of the scattering of reports.

Though enlarged glands of the tracheobronchial region due in part to tuberculosis were mentioned as early as the middle of the eighteenth century, it remained for LeBlond,[87] in 1824, to give the first adequate description of cases of sudden death from rupture of these glands into the adjoining air passages in children. His reports dealt, however, with the autopsy observations after an illness of several months' duration and are not included in this series. Perforation of the glands into the trachea in an adult had been described by Cayol[86] in 1810. Becker,[88] of Berlin, added an important contribution in 1826. Laennec[89] mentioned that the "physician of the Children's Hospital" had ofter encountered this condition. It was made the subject, from time to time of theses at the University of Paris and elsewhere.

The cases reported in the present survey of the literature have been selected in a definite fashion. Only those have been included that showed adequate clinical or postmortem evidence of respiratory obstruction from rupture of tuberculous tracheobronchial glands into either the trachea or the main bronchi in children under 13 years of age. Those cases have been excluded in which there was (1) compression without rupture, (2) rupture into secondary or tertiary bronchi only, (3) "silent" rupture found at autopsy following a chronic course in which no acute asphyxia had been present or (4) perforation into the main air passages in a person of 13 years or over. A total of ninety-four cases in the foreign literature is impressive and leads one to suspect that in this country similar episodes may have passed unrecognized, for I have failed to find a complete report of a case in a child in the American literature.

Attacks have occurred with or without preceding muscular activity or exertion; in a few cases the use of the muscles of deglutition alone appeared to have precipitated the attack. However, it is apparent from the literature that the true cause of sudden death in these cases often remains obscure in the absence of postmortem examination. Several of the included cases occurred in apparently healthy children who, while eating an apple or drinking coffee, for instance, were suddenly seized with choking spells and suffocated before a physician could be summoned. The consensus, in the absence of postmortem confirmation, was that the "food had gone down the wrong way." In other instances the episode was wrongly attributed to thymic enlargement or to so-called status lymphaticus. Autopsy showed that a caseous gland had ruptured into the main air passages and that its contents had become lodged in the glottis, causing complete respiratory obstruction.

The first description of recovery from one of these asphyxial attacks was published by Oekonomides [1] in 1882. In all, nineteen recoveries have been described, and these, together with the present, twentieth, case, are listed in table 1. In ten instances the tuberculous nature of the obstructing material was established by demonstration of the organisms in stained smears or by definite histologic evidence. In the others the author was usually satisfied from the gross appearance of the caseous material recovered that it was of tuberculous origin, though occasionally, as in Nachod's [5] case and in Erdely's [10] second case, the attempt to demonstrate tubercle bacilli was unsuccessful. In Petersen's [2] case a family history of tuberculosis was cited to support the diagnosis. Adler's [9] report raises a legitimate doubt as to the tuberculous etiology, since no direct evidence of the specific infection was mentioned and since the pus expectorated had a foul odor; the case is included because the original observer, who was in the strongest position to judge, regarded it as tuberculous. The tuberculous nature of the fatal cases

TABLE 1.—*Data on Cases in Which the Patient Recovered*

| Author and Date | Age | Sex | Salient Points in History | Physical and Operative Findings | Special Treatment Instituted | Evidence of Tuberculosis | Comment |
|---|---|---|---|---|---|---|---|
| Oekonomides [1] 1882 | 11 years | Boy | Sudden tightening in chest; began to cough; expectorated plug of material | ..... | None..... | Caseous tuberculous gland; tubercle bacilli demonstrated | Recovered rapidly; no further trouble |
| Petersen [2] 1885 | 6 years | Girl | Bronchitis, followed by coughing and asthmatic attacks, increasing in severity; four months later, a severe, sudden asphyxial attack | Inspiratory stridor, dyspnea, hoarseness | Tracheotomy with insertion of a Nélaton catheter | Tuberculous glandular material; tuberculous family history | Pieces of gland removed, in all an amount equivalent in size to a pigeon's egg; complete recovery |
| Voelcker [3] 1895 | 4 years | Girl | Measles (spring, 1892); four weeks after attack of measles, sudden dyspnea with swelling neck region, spreading upward to eyes and downward to navel; dyspnea disappeared, followed by expectoration of pus and blood for three weeks | Dyspnea disappeared as subcutaneous swelling increased | None..... | ..... | Conclusion: gland discharged contents into trachea; swelling due to escape of air into subcutaneous tissue |
| Fronz [4] 1897 | 8 years | Girl | Dyspneic and cyanotic attacks for an indefinite period; temporary relief following tracheotomy | Tuberculous infiltration of right lower lobe from aspiration | Tracheotomy and suction | Tubercle bacilli in caseous material expectorated | Author stated that perforation of main bronchus caused attacks |
| Nachod [5] 1897 | 6½ years | Boy | Cough for 5 days with hoarseness, marked dyspnea and stridor during both phases of respiration | Inspiratory and expiratory stridor; breath sounds of right lung decreased | Tracheotomy; pieces of gland removed by forceps | Tuberculous glandular material histologically; no tubercle bacilli recovered | Granulating wound in right main bronchus; bronchitis and pleurisy, which healed completely |
| Schaldemose [6] 1902 | 4 years | Boy | Chest infections at ages of 6 weeks and 2½ years; onset 5 months before admission cough and noisy respiration; after 2 months presented "mucus on the lungs"; lost weight | Cyanosis of lips and cheeks; marked dyspnea on exertion, later constant and accompanied by expiratory stridor; laryngoscopy gave negative results; rhonchi heard all over chest; expiratory murmur very faint | Tracheotomy tube worn 2 months with relief; attack of cough and dyspnea 3 days after its removal relieved by inserting forceps through tracheal incision and dislodging a caseous mass | Examination of pea-sized mass; cheesy "glandular" fibers; tubercle bacilli found | Many caseous masses expelled; cannula removed 4 weeks after incision of trachea; patient completely well about 4 months after rupture |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Jundell [7] 1904 | 11 years | Boy | Afternoon fever, night sweats; fainting spells; coughing attacks, pertussis-like sounds and sudden choking spells with expectoration of fetid masses | ..... | None | Caseous tuberculous glandular material histologically; tubercle bacilli demonstrated | Masses in all equaled size of a walnut; fairly prompt recovery |
| Pollak [8] 1906 | 4 years | Boy | Dyspneic attacks for 2 months, increasing in severity | Tracheal stenosis seen by tracheoscopy | Intubation not effective; tracheotomy; relief accompanied spontaneous expectoration of necrotic débris through cannula | Tuberculous material recovered | Cannula removed in 15 days; patient completely well 2½ months later |
| Adler [9] 1906 | 5 years | Boy | Difficulty in breathing, recurring 1 week after intubation | Breath foul after tube was removed; spreading infiltration of left lung developed which eventually cleared | Intubation for suspected croup; tracheotomy | ..... | Much foul-smelling pus removed following tracheotomy; author stated that patient recovered because contents of gland were completely fluid |
| Erdely [10] 1906 | 6 years | Boy | Extreme dyspnea for 3 days; no cough or constitutional symptoms | Tumor-like protrusion just above bifurcation discharging whitish caseous material | Intubation not effective; tracheotomy; three bronchoscopies through tracheotomy opening with removal of caseous material once | Tuberculous material the size of a pea removed | Suffocating attacks recurred after tracheotomy; not stated when tracheotomy tube was removed; patient reported well 1 year later |
| Erdely [10] 1906 | 2 years | Boy | Dyspnea for 24 hours; similar attack 6 months previously | Dyspneic attacks subsided immediately on removal of pieces of tissue | Tracheotomy gave no relief; bronchoscopy through tracheotomy opening with removal of obstructing mass twice; four bronchoscopies in all | Tuberculous material removed; no tubercle bacilli found | Mass in right main bronchus; granulation tissue excessive in amount; cannula in place 5 weeks; gained weight well |
| Schmiegelow [11] 1908 | 2½ years | Boy | Repeated attacks for 2 months of cough and gasping respirations, increasing in severity | Cyanosis during choking attacks | Tracheotomy; bronchoscopy through wound, with removal of masses seen at bifurcation | Tubercle bacilli found in masses | Rapid recovery |
| Hirschland [12] 1909 | 3 years | Boy | Sudden choking spells | Rupture localized 1.5 cm. below bifurcation in right main bronchus | Tracheotomy with lower bronchoscopy; suction through tracheotomy tube removed glandular material | Tuberculous glandular material | Granulating focus seen |

TABLE 1.—*Data on Cases in Which the Patient Recovered—Continued*

| Author and Date | Age | Sex | Salient Points in History | Physical and Operative Findings | Special Treatment Instituted | Evidence of Tuberculosis | Comment |
|---|---|---|---|---|---|---|---|
| Dina [13] 1909 | 5 years | Boy | Asphyxial attack | Oval caseous mass found in trachea; mucous discharge followed removal of mass; cough persisted for a while | Intubation; tracheotomy; mass removed from trachea | Tuberculous material | Rupture probably in left main bronchus near bifurcation; rapid recovery |
| Mann [14] 1920 | 6 years | Boy | Breathlessness for several days; sudden attack of dyspnea and cyanosis three days previously | Swelling into trachea on right side; caseous material discharging | Tracheotomy; piece of material size of hazelnut wiped away with swab | Tuberculous material | Granulating focus seen; rapid recovery |
| Mann [14] 1920 | 2 years | Boy | Severe dyspnea for 24 hours; similar attack 6 months before; persistent cough between these attacks | Diminished expansion of right side of chest; entrance to right main bronchus obstructed by mass the size of a bean | High tracheotomy; removal of mass by forceps; bronchoscopy | Tuberculous material | Bronchoscopy showed perforation into right main bronchus and cavity |
| van Gilse [15] 1922 | 3 years | Boy | Fever and coughing attacks for an indefinite period; father died of pulmonary tuberculosis | Diminished breathing in left lower lobe; sonorous breathing; roentgen examination showed little air in lower lobe; no foreign body; no enlargement of hilar glands | Superior bronchoscopy and tracheotomy; inferior bronchoscopy through tracheotomy opening; removal of mass through opening | Mantoux test strongly positive; tissue revealed tubercles and tubercle bacilli | Immediate improvement; three years later, patient well; lungs normal; mediastinal glands enlarged |
| Huizinga [16] 1931 | 8 years | Boy | Cough for months, thought to have started when eating a pear, followed by dyspnea and stridor on exertion | Absence of breath sounds on right side; caseous masses on lateral wall of right main bronchus | Bronchoscopy with removal of tissue; immediate improvement | Pirquet test positive; tissue removed histologically tuberculous | Rupture not found at second bronchoscopy 9 months later; no roentgenographic evidence of tuberculosis at this time; complete recovery |
| Malmberg [17] 1932 | 4 years | Boy | Sudden, severe coughing attack in a patient known to have pulmonary and mediastinal lymph node tuberculosis | Roentgen examination showed enlarged mediastinal glands (tuberculous) | None; grayish-red, hard plug coughed up, looking like partly cooked meat | Tuberculin test positive; tubercle bacilli found in section; histologically, tuberculous lymph node architecture | No spread of pulmonary infection; patient clinically well 2 years after the attack |
| Author's case 1934 | 16 months | Boy | Sudden dyspnea, with cyanosis and stridor, in a tuberculous patient | Enlarged mediastinal lymph node shown by roentgen examination | Intubation not effective; tracheotomy with removal of caseous plugs by suction through tube | Tubercle bacilli demonstrated in caseous material removed; Mantoux test positive | Bronchoscopy demonstrated site of rupture on medial side of right bronchus, close to bifurcation; patient clinically well 1½ years after the attack; youngest patient reported |

included in this survey rests on postmortem in addition to clinical evidence.

The sex distribution of the cases is given in table 2, which shows the condition to be 3.75 times as common in boys as in girls—a difference which is presumably significant, though its explanation is obscure.

In eighty-seven cases (92.5 per cent of the total number) the age was given. The youngest patient [24] was 5 months of age; * the oldest, 12 years. Fifty-five cases (63.2 per cent) occurred between the ages of 3 and 7 years. Thirty-nine of the sixty cases in boys (65 per cent) in which the age was noted occurred during these years. Twenty of the eighty-seven patients were 4 years of age. This is also the average age.

As Mann [14] stated, it is definitely rare to find such an acute asphyxial episode in an adult. Over 90 per cent of the reported cases have occurred in children. The reason is readily understood when one considers that tuberculosis in childhood is predominantly a glandular disease, in contrast to the parenchymatous involvement of adult life.

TABLE 2.—*Sex Incidence of the Cases Reported*

| | Boys | Girls | Sex Not Given | Total |
|---|---|---|---|---|
| Patients who survived | 17 | 3 | 0 | 20 |
| Patients who died | 43 | 13 | 18 | 74 |
| Total | 60 | 16 | 18 | 94 |

Dyspnea, cyanosis and stridulant breathing are the symptoms most frequently encountered in the reports in the literature. "Choking fits" accompanied by cyanosis are commonly described, while cough appears less frequently. The picture is that of impending suffocation. The most common finding on examination of the chest has been faintness or almost complete absence of the respiratory murmur. Atelectasis has often been suggested as a possible diagnosis by the various examiners. The findings have been unilateral or bilateral, depending of course on the site of the

* My statement that my patient is the youngest of those who recovered is based on examination of the original case reports. Two errors should be mentioned at this time.

Comba's [66] original case report was abstracted in the *Archiv für Kinderheilkunde* (**44**:416, 1906) and through an error the patient's age was given as 11 weeks instead of 11 years as stated by Comba. Schmiegelow [77] apparently used this erroneous abstract, for in his discussion he stressed the youth of Comba's patient.

Ballard [22] originally reported a fatal outcome in a boy 5½ months of age, Fuller having been called in consultation. When the report was abstracted in the *Journal für Kinderkrankheiten* (**36**:298, 1861), the case was attributed to Fuller. Loeb [98] referred to this abstract and did not mention Ballard. To correct this error partially, the references are listed in the bibliography after Ballard's name, though they are cited in the various medical indexes as being by Fuller. Fuller [23] reported a fatal result in a girl 4 years of age.

obstruction. The first diagnostic impression has generally been that the condition was either laryngeal diphtheria or obstruction caused by an aspirated foreign body. Enlargement of the thymus has followed closely as a third possibility. It is interesting to note that the temperature remained approximately normal in the majority of the cases in which it was mentioned. Apparently fever is the exception rather than the rule.

Examination of the masses expectorated often furnished the first definite clue as to the true etiology in those patients who survived the first asphyxial attack. Emphasis should be placed on the value of studying the material that comes from the tracheotomy tube. In most of the cases which ended in cure some mention was made of such an investigation. The most common expression employed was "caseous glandular material."

In the fatal cases reported, the asphyxial attack itself was usually the immediate cause of death. In the cases of the patients who recovered, relief from the respiratory embarrassment was brought about in various ways: In four instances the obstructing material was coughed up spontaneously—occasionally, as in Malmberg's [17] case, in the form of a single discrete mass, but more often as smaller particles brought up from time to time over a period of several days. In fifteen, tracheotomy was performed; in four of these cases, including mine, intubation was carried out first but, proving ineffectual, was followed by tracheotomy. Seldom was this enough, for in eleven of the fifteen cases in which tracheotomy was required it was necessary to resort to additional measures to obtain relief from respiratory difficulty; in six this was effected by mechanical dislodgment or actual removal with forceps of obstructing material reached through the operative wound, while in five cases suction was successfully applied with a catheter passed through the tracheotomy tube. In one case relief was brought about by endobronchoscopic maneuvers without aid from tracheotomy. In four cases tracheotomy and bronchoscopy were combined at the time of the first asphyxial attack in the effort to bring relief, while in six bronchoscopy was performed at some later stage either for therapy or for observation of progress.

The literature, as well as my own experience, attests the value of tracheotomy and bronchoscopy in securing relief from the first asphyxial attack and in preventing secondary attacks. Paunz [105] has gone so far as to advocate more or less drastic operative procedures for the prevention of asphyxial episodes in cases in which a caseous node pressing from without on the main air passages causes demonstrable occlusion, without having actually broken through. His method is to effect an artificial rupture through a bronchoscope and thus to drain the gland or aid in the removal of its contents. He cited fifteen cases in which the patients were treated operatively, twelve ending in recovery and

two in death following a miliary dissemination, while one patient died of suffocation. He mentioned the marked prevalence of perforation on the right side and especially in the medial wall of the right main bronchus. He also referred to the frequency with which the interbifurcation gland is the particular source of obstruction. This method has not been generally adopted; it is aimed at the prevention of possible asphyxial attacks rather than at their treatment once the syndrome is at hand, and his case reports are not included in this study.

Several cases have been reported (Thompson,[28] Demme,[42] Gulliver [47] and Ord [48]) in which the child showed satisfactory improvement from the first symptoms of dyspnea only to succumb to a second seizure which did not occur until ten days or more after the first. In some of these cases tracheotomy had been performed in the effort to relieve the original dyspneic attack, but, the patient's symptoms subsequently abating, the tube had in the meantime been removed. The second attack under these circumstances is probably due both to stenosis, resulting from granulations at the point of rupture or at the site of tracheotomy, and to the continuous collection of thick phlegm and caseous particles at one of these points. Eventually the process leads to complete obstruction and repetition of the asphyxial attack.

The production of granulation tissue at the point of rupture is to be expected. It has been reported as varying from a small amount to almost enough to occlude the lumen of the air passage. From the bronchoscopic reports this reaction is known to persist in varying degrees for several weeks after the primary rupture. It slowly decreases in amount, as do the swelling and redness of the mucous membranes of the trachea and bronchi.

Bronchoscopy in the case here presented, performed nineteen days after tracheotomy, showed much granulation tissue at the site of the tracheal wound, which bled easily when touched. There was also a profuse discharge coming from both bronchi at the time. Another bronchoscopy one month later, nearly seven weeks after rupture, showed excessive granulating tissue over the site of rupture, but the granulations at the tracheotomy wound were much less conspicuous.

It appears indubitable that the condition of the air passages, so far as patency of the lumen, amount of granulation tissue, discharge, etc., as seen through a bronchoscope, are concerned, is the chief criterion for removal of the tracheotomy tube. Even though the patient is entirely free from respiratory trouble at the time, it seems to be a grave error to feel that danger has been eliminated until it is definitely known that the lumens of the respiratory passages are free from obstructing masses.

This unfortunate lesson was demonstrated in the case of my patient when the tube was removed on the eighth day following the first tracheotomy. The course was uneventful for the next ten days, though

in retrospect one can perceive that warning signs existed during that period. It was finally necessary, after a few days of attacks of cyanosis, dyspnea and extreme physical embarrassment on the part of the patient, not to mention marked feelings of anxiety and apprehension on the part of the hospital staff, to repeat the tracheotomy lest asphyxial death should take place. The tube then remained in place about one hundred days. Contraction of scar tissue at the site of operation may eventually interfere with the replacement of the tube, but the air passages are usually not impinged on by the time this has occurred.

The conclusion from my own experience and from the results in the majority of cases of this type is that the principal danger from the use of a tracheotomy tube lies in its too early removal. It is important to search the expectorated material microscopically, not only for the security of a definite diagnosis, but later also as a guide to prognosis and to further treatment. It seems wise to keep the tracheotomy tube in place as security against a recurrence of asphyxia as long as tubercle bacilli can be found in the discharge. Patients who have been allowed to leave the hospital a short time after their apparent recovery, and who have later died suddenly, might conceivably have fared better if kept under close observation for a longer time; and the persistence of organisms may well be the safest criterion to follow in judging whether the threat of acute asphyxia is still present. It is easy to see these mistakes in retrospect, but it remains to profit from them and to avoid their repetition. Tubercle bacilli were found in the material removed by suction in our case nearly three months after the primary rupture. They could not be found a short time later, before the tube was removed.

Bronchogenic spread of the tuberculous infection following recovery from the asphyxial episode is a possible complication, although surprisingly rare in the present series of cases. The therapeutic measures used for relief may implant or activate a nontuberculous infection which displays itself as bronchitis or as pneumonia and which, furthermore, may play a part in precipitating additional attacks of cyanosis by causing an increase in the amount of tracheal secretion and a consequently greater opportunity for mechanical obstruction. Other complications described are not peculiar to this particular syndrome but may follow tracheotomy for any sort of indication. (I refer here especially to subcutaneous emphysema and pneumothorax.) In Voelcker's [3] case subcutaneous emphysema accompanied spontaneous relief from respiratory obstruction.

The percentage of patients who recover cannot be given accurately from this study. A prognosis based on the figures reported here would be too optimistic because of the selection of favorable cases for reporting, already alluded to. Ebert [72] probably gave the most accurate figure when he mentioned that in only nine of one hundred and forty-four

reported cases of perforation of caseous glands into the neighboring air passages in persons of all ages did the patient survive—a percentage of recovery of 6.2.

SUMMARY

Progressive caseation of a tracheobronchial lymph node may cause it to erode through the wall of the trachea or of a primary bronchus and to discharge its contents into the lumen of the respiratory tree, giving rise to symptoms of mechanical obstruction to respiration As a rule, the glands involved have formed part of the primary complex, and the symptoms referable to the tuberculous infection itself have been insignificant or absent, the asphyxial episode coming on suddenly out of an apparently clear sky. In the great majority of the reported cases, which are listed in the bibliography, asphyxia has been acute and fatal; in a smaller number, premonitary symptoms or signs have brought the patient under observation and made it possible to institute effectual therapeutic measures for relief. One such case is described in detail, and a tabular review is offered of all the other cases found in the literature in which the patient was relieved of this form of respiratory obstruction, either through being able spontaneously to dislodge the mass or through therapeutic intervention

In my patient, a boy of 16 months, moderate dyspnea of infraglottic origin brought the child to the hospital and remained unchanged for a few days until, with the sudden discharge of the semisolid contents of a tuberculous mediastinal lymph node into the tracheobronchial tree, acute asphyxia developed. The immediate symptoms were relieved by tracheotomy and aspiration of the tracheal contents. In spite of repetition of the asphyxial episode, the patient ultimately made a satisfactory recovery, without extensive spread of pulmonary tuberculosis.

The literature on such accidents occurring in subjects under 13 years of age is briefly reviewed, comprising reports of ninety-four cases, with twenty recoveries. The condition occurs most frequently in boys between 3 and 7 years of age. Requisite measures for diagnosis and treatment are discussed. It is felt that such episodes are more common than the published reports indicate, particularly since this is the first case of the kind reported in the American literature.

The seriousness of this complication warrants its recognition by all. Though fortunately rare, it should be included among the diagnostic possibilities, along with diphtheritic and other forms of laryngitis, an aspirated foreign body, thymic enlargement, laryngismus stridulus, asthma and the like, when dyspnea with stridor and cyanosis is encountered.

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# Pediatric Biographies

## JOHANNES LANGE
### 1485-1565

### A NOTE ON THE HISTORY OF CHLOROSIS

JOHN RUHRÄH, M.D.
BALTIMORE

Johannes Lange was born at Löwenberg in Silesia. He studied at Leipzig, where he was granted his master's degree in 1514. In a circle of young men, to whom he lectured on Pliny, was Joachim Camerarius. Determining on the study of medicine, Lange went to Ferrara, where he studied under Leonecenus, and later to Bologna, where he studied surgery with Carpi. He received his degree in Pisa in 1522, and then returned to Germany to enter the service of the Kurfürst of the Pfalz. For forty years he served five regents in the position of Archiater to the Palatinate. For thirty-seven years he accompanied the Kurfürst Friedrich II in his travels over Europe and took part in two wars against the Sultan Suleiman. He died in Heidelberg at the age of 80, on June 21, 1565.

Apart from some short articles referred to by Haller, his writings consist of letters which were published with the title, "Medicinalium epistolarum miscellanea, varia et rara" (Basle, 1554 and 1560; Frankfort, 1589, 1605 and 1689 and Hannover, 1705). The first edition contained 83 letters and the last 150.

Lange was the child of his age, tending to revere the ancients but combating the hocus-pocus of the charlatans. He was against many of the superstitions of the day and wrote much about the uselessness and dangers of diagnosis by uroscopy. A discussion of his letters by Viktor Fossel may be read in the *Archiv für Geschichte der Medizin*.[1]

Lange,[2] in his "Epistola," has left what is doubtless the earliest account of chlorosis, entitled "De morbo virgineo," or disease of virgins. It is to be found in the 1554 edition on page 74.

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DE MORBO VIRGINEO [3]

EPISTOLA XXI

. . . You will have complained to me, your faithful companion, that your first born daughter, Anna, & now sad, is desired in marriage by many suitors, of great excellency and illustrious birth, and also with an abundance of wealth, descended by ancestry from your forebears not from your inferiors; whom you are compelled to refuse because of the weakness of your daughter. Neither is this as obnoxious to you, as that thus far none of the Doctors have been able to

JOHANNES LANGE

1485-1565

explain the internal cause & essence of her disease, and at the same time prescribe the treatment. For one says it is cardalgia, another throbbing of the heart, this one indeed dyspnoea, that one suffocation of the womb: nor are those wonting, who suspect a loathing of the stomach from disease of the liver, the differing judgment of them concerning the illness of your daughter, you say proves that you are quite perplexed, nor are you able to tell what indeed should be done.

3. The translation is by Ralph H. Major in his "Classic Descriptions of Disease" (Springfield, Ill., Charles C. Thomas, Publisher, 1932, p. 445), and is used by permission.

Since you demand this opinion of the disease of the girl, and dependable advice concerning marriage, because of our old friendship, and at the same time you rightly ask with what kind of disease is she afflicted: since the qualities of her face, which in the past year was distinguished by rosiness of cheeks and redness of lips, is some how as if exsanguinated, sadly paled, the heart trembles with every movement of her body, and the arteries of her temples pulsate, & she is seized with dyspnoea in dancing or climbing the stairs, her stomach loathes food and particularly meat, & the legs, especially at the ankles, become edematous at night. From these accidents indeed, & from the pathognomonic signs of the disease, which betray the cause and nature of the disease, point out its treatment, I marvel that old physicians do not know the cause & nature of the disease. Although indeed they have not mentioned its name, which moreover contributes nothing to its treatment, that is nothing of importance.

There are many illnesses in the catalogue of diseases, lacking a name & not a treatment. Nor has this disease a proper name, as much as it is peculiar to virgins, might indeed be called "virgineus," which it is the custom of the matrons of Brabont to call white fever, or pale face & the fever of love: since every lover becomes pale, & this color is proper for a lover, although a fever very rarely is present. But this disease frequently attacks virgins, when now mature they pass from youth to virility. For at this time, by nature, the menstrual blood flows from the liver to the small spaces & veins of the womb: which when from the narrow mouths, which are not yet distended, also obstructed by thick & crude humors, & finally from the thickness of the blood, cannot escape: then carried backwards through the vena cava and the larger arteries flows to the heart, liver, diaphragm & veins of the diaphragm: also a good part is distributed to the head, & grave accidents appear in the viscera, dyspnoea, a tremulous throbbing of the heart, inflation of the liver, nausea of the stomach, cardalgia: not rarely epilepsy with loss of senses, & delirium.

Although Hippocrates in the book on diseases of Virgins declares: Virgins, he says, to whom the time of marriage comes, and are now mature, are afflicted with imaginary terrors of spectres, especially when the menses appear, for before this, they are not at all badly affected, afterwards indeed the blood in the small spaces of the womb, as it were escaping, drips and falls, since the obstructed mouths were the places of egress, and the blood abundant from the foods & the growth of the body, collected there, is present in large quantity and whence it flows distending the opening of the veins, the heart beyond its power moves up to the septum transversum & diaphragm, the heart itself does not hold out & becomes torpid, then from this torpidity the patient becomes foolish and delirious. It is certainly no wonder since the liver is not cleansed of the filthy blood of the menses, & by it the veins of the diaphragm are stopped up, the viscera of the abdomen swell, & the diaphragm is contracted (as in hydrops), then a difficulty in breathing appears, as Galen points out in his third book on Dyspnoea, where he says in general: If an internal tumor or pain has existed in the abdomen, then respiration is shallow & rapid.

After this the heart, stomach & liver, the veins & arteries of which are connected by juice & branches, as by a common bond, these filled & obstructed indeed by the gross blood, crammed with spirits and vapors, so that the heart casts these out & expells them, that it may not be choked by the great numbers of arteries & struggles with the movement of contraction & trembles all over. . . .

Finally, whether your daughter ill with this affection ought to marry, & what should be the treatment of it, see I shall communicate the trusty advice from the rich store of the medicine of Hippocrates, who says in his book on diseases of

Virgins: the cure of this disease is venesection if nothing hinders. I therefore say, I instruct, virgins afflicted with this disease, that as soon as possible they live with men & copulate, if they conceive they recover, if indeed they be not attacked by this disease in puberty, then it attacks a little later unless they have been married. Moreover indeed of the married, very many are sterile. With this most wholesome advice of the divine Hippocrates, if medicines produce menses and loosening up obstructions, if you produce a thinning of the thick blood, you can discover & devise nothing more powerful than this. In the treatment of this disease of virgins I have never been deceived or my hopes frustrated. Wherefore, be of good courage, you shall give away your daughter: also I shall be present at the nuptials with pleasure. . . .

# Pediatrics in Art

## DELOUSING THE HEAD

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There are a number of paintings by various artists depicting the rather homely scene of cleaning the head of unwelcome visitors. None of these exceeds in simplicity and charm that of Murillo, which is

"An Old Woman Cleaning the Head of a Boy," by Murillo.

entitled "An Old Woman Cleaning the Head of a Boy." It hangs in the old Pinakothek in Munich. The old woman is actively engaged in her task, while the careless little Spaniard eats his bread and plays with his puppy. The old woman has laid aside her distaff and spindle to give her full attention to the boy.

Murillo (1617 to 1682) was born at Seville. He worked for a while in Madrid and then returned to Seville, where he married a wealthy woman and lived in considerable state. His is a soft, smooth art which is sometimes highly praised and not infrequently belittled. More than forty of his compositions hang in the Louvre in Paris, among them what is regarded as his *chef-d'oeuvre,* "The Immaculate Conception," which was acquired in 1852 from the sale of the collection of Marshall Soult for 26,612 pounds. The photograph reproduced here is by Bruckmann of Munich.

# News and Comment

## GENERAL

**Physicians Certified by American Board of Pediatrics.**—At the meeting of the American Board of Pediatrics held June 9 and 10 in Cleveland, the following applicants were certified.

Group I: I. A. Abt, Chicago; C. A. Aldrich, Winnetka, Ill.; N. N. Allen, Houston, Texas; Samuel Amberg, Rochester, Minn.; L. O. Ashton, New York; P. S. Astrowe, Kansas City, Mo.; O. L. Baldwin, Columbus, Ohio; O. Barbour, Peoria, Ill.; P. F. Barbour, Louisville, Ky.; E. J. Barnett, Spokane, Wash.; G. E. Baxter, Chicago; P. W. Beaven, Rochester, N. Y.; W. W. Belford, San Diego, Calif.; N. C. Bender, Buffalo; P. B. Bender, Philadelphia; B. Bernbaum, Detroit; Robert Blessing, Evanston, Ill.; C. E. Boynton, Atlanta, Ga.; W. N. Bradley, Philadelphia; J. W. Bruce, Louisville, Ky.; W. P. Buffum, Providence, R. I.; H. C. Carpenter, Philadelphia; J. C. Carter, Indianapolis; H. Casparis, Nashville, Tenn.; L. I. Clark, Toledo, Ohio; W. E. Collins, Kalamazoo, Mich.; E. P. Cook, San Jose, Calif.; T. B. Cooley, Detroit; F. J. Corper, Chicago; W. C. Davison, Durham, N. C.; H. P. Dawson, Montgomery, Ala.; A. G. DeSanctis, New York; H. F. Downing, Cincinnati; J. Dunn, Davenport, Iowa; J. I. Durand, Seattle; H. W. Elghammer, Chicago; M. M. Eliot, New Haven, Conn.; H. K. Faber, San Francisco; E. S. Fish, Los Angeles; R. G. Flood, San Francisco; R. P. Forbes, Denver; J. M. Frawley, Fresno, Calif.; E. Friedman, Boston; F. P. Gengenbach, Denver; S. D. Giffen, Toledo, Ohio; O. L. Goehle, Lakewood, Ohio; S. Goldberg, Philadelphia; T. D. Gordon, Grand Rapids, Mich.; J. V. Greenebaum, Cincinnati; S. McC. Hamill, Philadelphia; H. H. Harrison, Asheville, N. C.; W. M. Hartshorn, New York; C. Harvey, Pontiac, Mich.; J. E. Harvey, Pasadena, Calif.; H. F. Helmholz, Rochester, Minn.; T. C. Hempelmann, St. Louis.; S. C. Henn, Chicago; J. A. Henske, Omaha; C. Herrman, New York; H. L. Higgins, Boston; L. F. Hill, Des Moines, Iowa; E. G. Hummel, Camden, N. J.; F. E. Johnson, New York; A. D. Kaiser, Rochester, N. Y.; S. R. Kaliski, San Antonio, Texas; S. Karelitz, New York; R. L. J. Kennedy, Rochester, Minn.; C. G. Kerley, New York; LeGrand Kerr, Brooklyn; R. A. Knox, Washington, Pa.; Benjamin Kramer, Brooklyn; F. I. Krauss, Chatham, N. J.; G. N. Krost, Chicago; J. S. Leopold, New York; S. Z. Levine, New York; D. J. Levy, Detroit; J. I. Linde, New Haven, Conn.; J. G. Logue, Williamsport, Pa.; H. Lowenburg, Philadelphia; R. T. Incas, Shreveport, La.; W. P. Lucas, San Francisco; H. O. Lussky, Evanston, Ill.; C. P. Mangum, Richmond, Va.; C. W. Martin, Far Rockaway, N. Y.; D. D. Martin, Tampa, Fla.; E. W. May, Detroit; K. M. Mayer, Chicago; J. Meyer, Birmingham, Ala.; E. C. Mitchell, Memphis, Tenn.; J. C. Montgomery, Detroit; E. E. Moody, Los Angeles; H. L. Moore, Dallas, Texas; J. L. Morse, Boston; G. F. Munns, Winnetka, Ill.; J. E. McClelland, Cleveland; A. L. Newcomb, Chicago; S. Nichols, Asbury Park, N. J.; P. Nicholson, Ardmore, Pa.; Joseph Palma, Honolulu, T. H.; A. H. Parmelee, Oak Park, Ill.; M. G. Peterman, Milwaukee; E. S. Platou, Minneapolis; R. M. Pollitzer, Greenville, S. C.; P. S. Potter, Berkeley, Calif; C. M. Pounders, Oklahoma City; H. B. Pryor, San Francisco; B. Reading, Galveston, Texas; J. L. Reichert, Chicago; O. Reiss, Los Angeles; R. K. Rewalt, Williamsport, Pa.; A. L. Richardson, Detroit; F. G. Riley, Meridian, Miss.; M. H. Roberts, Atlanta, Ga.; E. E. Rodenheiser, Upper Darby, Pa.; E. H. Rohlfing, St. Louis; F. C. Rodda, Minneapolis; P. Rosenblum, Chicago; J. W. Rosenfield, Portland, Ore.; L. T. Royster, University, Pa.; John Ruhräh, Baltimore; L. W. Sauer, Evanston, Ill.; F. W. Schultz, Chicago; E. H.

Schorer, Kansas City, Mo.; L. C. Schroeder, New York; E. G. Schwarz, Fort Worth, Texas; H. Schwarz, New York; A. J. Scott Jr., Los Angeles; R. G. Sharp, San Diego, Calif.; E. B. Shaw, San Francisco; A. A. Shawkey, Charleston, W. Va.; J. Signorelli, New Orleans; J. F. Sinclair, Philadelphia; A. deG. Smith, Washington, D. C.; R. M. Smith, Boston; T. C. Smith, Louisville, Ky.; V. W. Spickard, Seattle; W. C. A. Steffen, Flushing, N. Y.; J. L. Stein, Brooklyn; W. B. Stewart, Atlantic City, N. J.; P. M. Stimson, New York; V. E. Stork, Los Angeles; H. C. Stuart, Boston; J. M. Sturtevant, New York; H. E. Thelander, San Francisco; A. J. Thornton, San Diego, Calif.; O. N. Torian, Indianapolis; I. H. Tumpeer, Chicago; R. M. Tyson, Philadelphia; P. Van Ingen, New York; B. S. Veeder, St. Louis; J. R. Vonachen, Peoria, Ill.; P. C. Waldo, Oak Park, Ill.; A. A. Walker, Birmingham, Ala.; J. H. Wallace, Oak Park, Ill.; T. M. Watson, Greenville, N. C.; E. S. Wegner, Lincoln, Neb.; P. J. White, St. Louis; S. J. Wilson, Brooklyn; G. H. Woltereck, Baltimore; C. W. Wyckoff, Cleveland; Joseph Yampolsky, Atlanta, Ga.; G. E. Zimmerman, Sioux Falls, S. D.

Group II: P. S. Barba, Philadelphia; I. R. Cohn, Toledo, Ohio.; E. E. Martmer, Detroit; L. T. Meiks, Indianapolis; G. R. Murphy, Elmira, N. Y.; J. F. Sander, Lansing, Mich.; J. C. Williams, Philadelphia.

Group III: R. W. Holt, Niagara Falls, N. Y.; J. F. Miller, Newark, N. J.; A. R. Nelson, Grand Rapids, Mich.

**Course in Pediatrics, University of Vienna.**—The usual course for practitioners will be held at the University of Vienna from Sept. 24 to Oct. 8, 1934. This will consist of the usual lectures and demonstrations by members of the pediatric group.

## PERSONAL

In commemoration of the completion of his thirtieth year of active service as a teacher of pediatrics, Prof. Rocco Jemma, director of the Pediatric Clinic, Royal University of Naples, Italy, and internationally famous pediatrician, has been accorded many signal honors by Italian pediatricians and the nation in general. *La pediatria,* outstanding Italian pediatric journal, has devoted an entire supplemental issue (June 1934) to the publication of congratulatory and commendatory expressions by outstanding pediatricians of every civilized country.

## UNIVERSITY NEWS

Dr. Edward B. Shaw has been promoted to associate clinical professor of pediatrics in the University of California Medical School, San Francisco.

Dr. Arvid Wallgren, professor of pediatrics and chief of the Children's Hospital in Göteberg, Sweden, who was the guest of the Pediatric Section of the American Medical Association and the American Academy of Pediatrics, delivered the Theodore B. Sachs lectures on tuberculosis at the University of Illinois on June 6 and 7.

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## CORRECTION

An error appeared in the title of the last abstract on page 1356 of the June 1934 issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN. The title of the article by Dr. Pernetta and Dr. Pinto, which appeared in the *Revista brasiliera de pediatría,* should read "Treatment of Tetanus by Intensive Serum Therapy," instead of "Treatment of Tetany."

# Abstracts from Current Literature

## Anatomy and Physiology

STRUCTURE OF THE BRONCHIAL TREE. E. HUIZINGA, Nederl. tijdschr. v. geneesk. **77**:3351 (July *22*) 1933.

Roentgenograms of the thorax made after the injection of iodized poppy seed oil 40 per cent into the lungs are an excellent means for studying problems of the anatomy and physiology of the thorax. A brief review is given of the conception of the structure of the bronchial tree, dating from Aeby. Recent investigations by Marcus and Hilber, who proved that the bronchial tree has a screwlike structure, are discussed in detail. These findings can be confirmed: In viewing the roentgenograms made after injection of poppy seed oil stereoscopically, a screwlike form is distinctly seen. In man a stem bronchus, as designed by Aeby, cannot be traced in the lower lobes of the lungs. The method lends itself excellently to the study of the anatomy of the bronchial tree and the respiratory movements. Peristaltic movements have not as yet been observed.

VAN CREVELD, Amsterdam, the Netherlands.

DIAMETER AND GROWTH OF THE BRONCHIAL TREE. E. HUIZINGA, Nederl. tijdschr. v. geneesk. **77**:3761 (Aug. 19) 1933.

On roentgenograms made following the introduction into the lung of iodized poppy seed oil 40 per cent the diameters of the trachea and bronchi can be measured, and their lumens can be calculated from these. The measurements in eighty-five persons from 2 years of age to adult age are given. Wide individual variations are found. The relations between the trachea and the right and left bronchi are fairly constant; in young children the left bronchus is relatively narrower. The entire air passage is almost tubular; after the branch for the upper lobe is given off the bronchus, especially the right one, tapers conically.

The trachea grows in such a way that its diameter bears a constant relation to the size of the lungs; the somewhat unequal rate of growth of the lungs asserts itself. By comparing these measurements with those of other parts of the body, one obtains the formula: The diameter of the trachea is one fiftieth of the circumference of the thorax. The lumen of the trachea is constantly proportionate to the surface of the body, not to its weight; the growth of the trachea proceeds, as might be expected, from its functioning as a tube for passage of gas.

VAN CREVELD, Amsterdam, the Netherlands.

## Pathology, Bacteriology and Biochemistry

RAPID PROCEDURE FOR THE PREPARATION OF AUTOVACCINES. MICHAEL CAMNER, Bull. Soc. de pédiat. de Iasi **3**:125 (Nov. *29*) 1932.

By using 100 per cent hydrogen dioxide as bactericide in addition to heat, Camner prepared autovaccines more rapidly than by the usual methods. The antigenic power of the vaccine is not diminished by hydrogen dioxide.

LEMASTER, Evanston, Ill.

DEGENERATIVE GRANULES IN NEUTROPHILS. J. MOLDAWSKY, Jahrb. f. Kinderh. **138**:44 (Jan.) 1933.

The author gives a historical account of so-called toxic granulations in neutrophils. He modifies Mommsen's method of staining as follows: Fix the film in methyl alcohol. Immerse for from one to one and a half hours in a mixture of

40 drops of Giemsa's stain in 10 cc. of acetate buffer of $p_H$ 5.4. This is made by mixing 21.6 cc. of normal sodium hydroxide solution and 27 cc. of normal acetic acid with water to make 1 liter. The basophilic granulations were observed in all the neutrophils of apparently healthy adults who had worked long near therapeutic roentgen ray apparatus, in those of all premature infants and in those of all children with diseases which stimulate leukopoietic tissue. They were not found in the neutrophils of children with certain types of anemia or in those of normal children.

CLAUSEN, Rochester, N. Y.

CIRCULATION TIME AND RATE OF BLOOD FLOW IN CHILDREN FROM SIX TO FIFTEEN YEARS OF AGE. H. SECKEL, Jahrb. f. Kinderh. **138**:56 (Jan.) 1933.

The circulation time was determined by the histamine rash method, the volume of blood by the dye method. Technical difficulties prevented the application of the former method to children of from 2 to 6 years of age. In thirty subjects the circulation time varied from seventeen to twenty-two seconds; it increased with age. It was possible to calculate the absolute volume of blood per minute as from 2.5 to 4 liters, the relative volume as from 140 to 100 cc. per kilogram of body weight and the volume per heart beat as from 30 to 57 cc. In a girl, 11½ years of age, suffering from exophthalmic goiter the volume per minute was greatly increased and the circulation time much diminished; the reverse was true in a case of obesity.

CLAUSEN, Rochester, N. Y.

A SIMPLE METHOD FOR THE DETERMINATION OF THE CALCIUM AND PHOSPHORUS CONTENT OF FECES. A. LICHTENSTEIN, Nederl. tijdschr. v. geneesk. **77**:4336 (Sept. 23) 1933.

A method of estimating the amount of calcium and phosphorus in 1 Gm. of fresh feces is described. The feces are weighed precisely and reduced to ash; the ash is dissolved in nitric acid; all the phosphorus is then precipitated by ammonium molybdate. The calcium content of the remaining fluid is determined by precipitating calcium in the form of the oxalate and titrating the oxalate by potassium permanganate after dissolving it in sulphuric acid. The amount of phosphorus can be determined in the molybdate residue, which is soluble in sodium hydroxide.

VAN CREVELD, Amsterdam, the Netherlands.

## Nutrition

INTRAPERITONEAL ADMINISTRATION OF VIOSTEROL IN MICE. JOHN W. SPIES and GEORGE P. LYMAN, Am. J. Physiol. **102**:527 (Dec.) 1932.

Viosterol in sesame oil was injected intraperitoneally into mice. This method was found efficacious in producing calcium deposits similar to the results obtained by workers using other methods of administration. The animals which lived more than thirty days after the beginning of the injections of viosterol revealed calcification in various organs, most marked in the lungs, aorta, kidneys and stomach.

NOURSE, Cleveland.

STUDIES IN THE B VITAMINS: III. EVIDENCE OF A THIRD VITAMIN B FACTOR IN YEAST ($B_4$) AS SHOWN BY GROWTH CURVES AND CLINICAL SYMPTOMS OF FIRST AND SECOND LITTER YOUNG OF MOTHERS RAISED ON SYNTHETIC $B_1$ AND $B_2$ DIETS. C. U. MOORE, H. B. PLYMATE and B. J. ANDREW, Am. J. Physiol. **102**:581 (Dec.) 1932.

The young of the first litter of rats fed on synthetic vitamin $B_1$ and $B_2$ diets required approximately double the maternal ration for normal growth after weaning. This amount proved inadequate for normal growth in the young of the second

litter. Both litters responded normally when yeast was added to the diet. Second litters could not be obtained until yeast had been added to the mother's diet for a period of one month before impregnation. These findings indicate the presence of a third vitamin B factor in yeast, which the authors identify with Reader's $B_4$.

NOURSE, Cleveland.

STUDIES IN THE B VITAMINS: VI. FURTHER CONSIDERATION OF PYLORIC OBSTRUCTION IN RATS. C. U. MOORE and H. B. PLYMATE, Am. J. Physiol. **102**:605 (Dec.) 1932.

Further observations on vitamin B are presented, which indicate that pyloric obstruction can be produced in rats fed diets containing inadequate amounts of vitamin B and that the $B_1$ fraction is evidently the factor at fault.

NOURSE, Cleveland.

FRESH AND DRIED YEAST AS SOURCES OF VITAMIN B. REED WALKER and E. M. NELSON, Am. J. Physiol. **103**:25 (Jan.) 1933.

Data are provided to show that the amount of vitamin B obtained by the rat from fresh compressed yeast cakes is approximately half that obtained from a similar cake that has been dried. Investigations of other workers showed that from 55 to 95 per cent of the number of live yeast cells ingested may pass through the stomach without being destroyed. This suggests an explanation of the inability of the rat to obtain as much vitamin B from fresh yeast as from the same material when dried.

NOURSE, Cleveland.

THE EFFECT OF THYROID FEEDING ON TISSUE RESPIRATION. R. W. GERARD and M. MCINTYRE, Am. J. Physiol. **103**:225 (Jan.) 1933.

Tissues from hyperthyroid dogs were found to consume more oxygen than tissue from control animals. These findings confirm the view that the thyroid hormone acts on cells to increase their metabolic activity. The one exception was thyroid tissue which showed diminished respiration of oxygen, supporting the view that the level of the hormone in the blood reaching the gland is an important means of regulating its activity.

NOURSE, Cleveland.

LACTOSE IN THE TREATMENT OF DIARRHEA AND VOMITING IN INFANTS, WITH ILLUSTRATIVE CASE REPORTS. SIMON M. SKOLE, Arch. Pediat. **50**:395 (June) 1933.

The writer reviews the results that he has obtained in the treatment of gastro-intestinal disorders in which lactose has been the sugar of choice. He believes lactose to be a safe, satisfactory and suitable sugar for use in cases of gastro-intestinal disturbances in infants, feeling that loss of weight can be avoided and the course and duration of the disease materially shortened by the use of lactose.

WADDELL, JR., University, Va.

A CRITICAL STUDY OF NINETY-SEVEN INFANTS FED ON LACTOGEN. RALPH N. SHAPIRO, Arch. Pediat. **50**:437 (June) 1933.

The writer reviews the results obtained in the cases of ninety-seven infants fed lactogen, the intervals of feeding varying from four to twenty-five weeks. On the whole, the results obtained show that lactogen, like many other proprietary foods, when fed in proper amounts will produce a normal gain in weight and correct certain conditions of underweight.

WADDELL, JR., University, Va.

INFLUENCE OF ULTRAVIOLET ON THE RÔLE OF OXYGEN IN MINERAL METABOLISM AND IMMUNITY REACTIONS. G. J. WARNHUIS, Arch. Phys. Therapy **14**:220 (April) 1933.

Oxygen in the human organism is subject to wide variation, partly because of the presence of hormones in the fluids of the tissues. A definite chemical similarity exists between the enzyme responsible for pigmentation of the skin and epinephrine. Evidence is presented for the probable influence of ultraviolet irradiation in activating these enzymes. The relationship of oxidative processes to mineral metabolism is considered and the hypothesis advanced that the action of ultraviolet irradiation on mineral metabolism may also be included as the result of a more normal and complete process of oxidation in which vitamin D is only an intermediary and not the primary factor.

KUGELMASS, New York.

CERTAIN EFFECTS OF ULTRA-VIOLET RADIATION ON THE CHEMICAL AND NUTRITIVE PROPERTIES OF BAKED PRODUCTS. J. W. READ and C. H. BAILEY, Cereal Chem. **10**:99, 1933.

Studies were made of the antirachitic potency imparted to soda crackers when irradiated with ultraviolet rays from a mercury vapor lamp for varying periods of time at a distance of 12 inches (30.48 cm.). The quantity of ultraviolet energy emitted under these conditions was 94 ergs per second per millimeter. Bone ash and "line test" methods of assay were used. The influence of ultraviolet rays in shortening the induction period of oxidative rancidity was established by means of odor intensity. Some lards contain an appreciable amount of vitamin D, while hydrogenated shortening and certain other lards do not appear to contain this vitamin. The technic adopted for the irradiation of soda crackers effected an antirachitic activation by an exposure for approximately ten seconds. This conclusion is based on the data on bone ash covering a 20 per cent level of intake of crackers irradiated on one side and applies to the use of hydrogenated shortenings and lards containing no vitamin D. Crackers made in the laboratory with irradiated shortening carried their antirachitic potency through the fermentation and baking processes.

KUGELMASS, New York.

WATER OR FAT? WATER RETENTION IN SO-CALLED ENDOCRINE OBESITY. L. G. ROWNTREE and L. A. BRUNSTING, Endocrinology **17**:377 (July-Aug.) 1933.

In two women, aged 20, obesity developed with gains of 30 and 60 pounds (13.6 and 27.2 Kg.) over a short period. In both the onset of menstruation occurred three or four years prematurely, and one menstruated at two week intervals. Because this patient also presented urticaria and angioneurotic edema, a derangement of water metabolism was suspected. Both patients were subjected to dehydration measures consisting of a reduced intake of fluid and the administration of ammonium salts by mouth and of mercurial diuretics. The weight quickly returned to normal, and it was possible to maintain it at this level as long as treatment was continued. It is suggested that the syndrome might be explained on a basis of an early excess of prolan A (the follicle-ripening hormone of the anterior lobe of the pituitary body), resulting in early puberty, and a subsequent excess of the pressor principle of the posterior lobe of the pituitary causing retention of water.

JACOBSEN, Buffalo.

THE INFLUENCE OF CALCIUM AND IODINE ON GROWING RATS. J. THOMPSON, Endocrinology **17**:537 (Sept.-Oct.) 1933.

The effect of diets containing varying amounts of calcium and iodine was observed in 250 rats over a period of seven months. It was found that the continuous consumption by the animals of diets low in iodine produced many clinical and pathologic manifestations of exophthalmic goiter: increased activity,

excitability and intake of food, failure to gain weight, disturbances in reproduction, exophthalmos, hypertrophy of the heart, enlargement of the thyroid gland and decrease in the percentage of bone ash and calcium content of the fat-free bones.

The addition of calcium carbonate resulted in greater enlargement of the thyroid gland, a greater decrease in the level of blood iodine and the development of degenerative changes in the parathyroid glands. The findings constitute additional evidence that an association exists between the calcium and iodine metabolism.

JACOBSEN, Buffalo.

VITAMIN B AND G CONTENTS OF DRY SKIMMED MILK AND DRY WHEY. R. C. BENDER and G. C. SUPPLEE, J. Dairy Sc. **15**:445, 1932.

The growth of rats was promoted equally by the addition of roller-dried skimmed milk or spray-dried whey to a basal diet, but the effect of commercial samples of dried whey varied markedly, probably because of the differences in the method of producing them. Diets containing milk products and supplemented with vitamin B by the addition of 2 per cent of rice polish invariably caused more rapid growth than diets containing milk products but no rice polish. The addition of the milk products and rice polish to basal diets after vitamin G was withheld for a period caused sharp increases in growth. The addition of about 12 per cent of dried skimmed milk or whey and 2 per cent of rice polish was sufficient to cause normal growth. Since rice polish has a high content of vitamin B and relatively little vitamin G, it is concluded that the vitamin B content of the milk products is relatively lower than the vitamin G content.

KUGELMASS, New York.

BASAL METABOLISM STUDIES IN OBESITY IN CHILDREN. CHARLES GILMORE KERLEY, J. Pediat. **2**:729 (June) 1933.

After studying a large number of obese children for several years, the author is of the opinion that obesity in children is usually of a temporary nature. The majority of fat boys and girls swing into line with their forebears about the time of puberty. Height, weight and bodily characteristics follow closely along ancestral lines. In some children a temporary endocrine dysfunction exists, and in the case of these gland therapy is of assistance. The omission of fats and sugars from the diet and the arrangement for bodily activities are all that appeared to be required to bring the obese child to a condition of normalcy, unless pronounced hereditary factors were present.

LEMASTER, Evanston, Ill.

ALIMENTARY INTOXICATION IN INFANTS: ACID-BASE EQUILIBRIUM WITH THE USE OF CONTINUOUS INTRAVENOUS THERAPY (PRELIMINARY REPORT). HENRY COHEN, PHILIP R. MILLER and BENJAMIN KRAMER, J. Pediat. **3**:299 (Aug.) 1933.

Nine infants with severe alimentary intoxication were treated by a continuous intravenous drip of 5 per cent dextrose in a saline solution, and the blood chemistry values were studied before, during and after treatment. Clinical improvement followed the establishment of diuresis which began from three to twenty-seven hours after therapy was started. As a rule the nonprotein nitrogen values were high at the onset, but decreased as the fluid and electrolyte balance was restored. Inorganic phosphorus readings were usually low or within normal limits. Calcium determinations showed no characteristic changes. In four severely dehydrated infants the serum protein reached 8 Gm. per hundred cubic centimeters or higher. In three of these cases a sudden drop in serum protein was accompanied by edema, necessitating cessation of the intravenous treatment and emphasizing one of the dangers of this form of therapy. In general the bicarbonate and chloride values varied inversely. Even when the chloride concentration increased, clinical

improvement occurred. The authors do not feel that there is much danger that the chlorides administered in the salt solution may exaggerate the acidosis. Intravenous therapy in intoxication allows a long period of gastro-intestinal rest, avoids physical and mental disturbance of the patient for an appreciable period and is a method whereby one is certain that the dextrose-saline solution is received and absorbed.

LEMASTER, Evanston, Ill.

THE PRODUCTION AND USE OF SOFT CURD MILK. MYRL MORRIS and GEORGE A. RICHARDSON, J. Pediat. **3**:449 (Sept.) 1933.

Sixty infants ranging in age from birth to 6 months were fed soft curd milk for from two to eight weeks. When fed to the point of satisfaction the infants took more of the soft curd milk than of ordinary cow's milk, owing probably to the lower energy value of the former. The infants who were fed soft curd milk increased in weight a little more than those fed diluted evaporated milk. The stools of the infants taking soft curd milk numbered from four to six daily and often contained large curds of casein. Analyses showed the soft curd milk to be lower in protein, energy value and buffer capacity than ordinary milk. Boiling lowered the curd tension of the milk formulas appreciably. The authors conclude that the benefits of soft curd milk do not warrant its special production for infant feeding.

LEMASTER, Evanston, Ill.

EFFECT OF ULTRA-VIOLET RAYS ON THE DERMATITIS-PREVENTING VITAMIN. ALBERT G. HOGAN and LUTHER R. RICHARDSON, Missouri Agric. Exper. Stat. Research Bull., no. 178, 1932, p. 3.

Attempts were made to produce a consistent dermatitis in rats. Satisfactory results were obtained by the use of ultraviolet rays from the mercury vapor arc in quartz to destroy the antidermatitis factors, though other features may also be of some significance. Forty-three animals received a ration presumably free from vitamin G, beginning at weaning time, and were maintained on this continuously as long as they lived. Their gains in weight were insignificant. Dermatitis developed in all within thirty-four days after weaning. The average period of survival after weaning was fifty-one days.

KUGELMASS, New York.

THE USE OF CARBOHYDRATES IN THE DIET AND TREATMENT OF INFANTS. ARTHUR F. ABT, Nebraska M. J. **18**:206 (June); 241 (July) 1933.

The digestion and metabolism of carbohydrates are discussed. It is pointed out that the actual amount of sugar which the infant can utilize differs according to the type of sugar, for instance, 8 Gm. of cane sugar per kilogram of body weight and 3.6 Gm. of lactose per kilogram of body weight. The optimal ratio of carbohydrate to fat is 1:2. While sugar meets the carbohydrate requirement of young infants, starch, in the form of cereals, vegetables and fruits, supplements the diet of older children. As sugar is converted into dextrose, the particular sugar used is unimportant from the metabolic standpoint. Possibly the absorption of calcium is aided by the use of lactose. The giving of excessive amounts of carbohydrates may lead to overweight, and an insufficient amount may lead to undernutrition. The importance of an insufficient amount in simple dystrophy and the danger of an excess amount in diarrhea are pointed out. The proper use of carbohydrates in decomposition and alimentary intoxication, as well as the parenteral use of dextrose in dehydration, is indicated. The use of sugar as a source of energy in vomiting and hypoglycemia and its use in the treatment of acute nephritis are discussed, as well as acidosis, "the sugar days" and the detoxicating action of dextrose in certain poisonings. Lastly, there is a brief discussion of the use of sugar in celiac disease and diabetes.

HAMILTON, Omaha.

INFLUENCE OF DIFFERENT LEVELS OF FAT INTAKE UPON MILK SECRETION. L. A. MAYNARD and C. M. MCCAY, New York (Cornell) Agric. Exper. Stat. Bull., no. 543, 1932, p. 3.

Removal of all but 1 per cent of the ether extract from grain mixtures containing from 6 to 7 per cent of crude fat and replacement with an equivalent amount of starch caused large decreases in yields of milk and butter-fat. Smaller decreases were caused by decreasing the fat content of grain mixtures to 3 per cent. The substitution of carbohydrate for fat in the ration was immediately reflected in the quality of the secreted fat, as shown by its higher iodine number. The lowering of the intake of fat, with the resultant decrease in the secretion of milk, was accompanied by a gradual lowering of the total fatty acids, the phospholipid fatty acids and the cholesterol of the blood plasma. The changes in the lipids exhibited a high degree of parallelism. The glucose values for whole blood, cells and plasma were unaffected by the changes in the ration.

KUGELMASS, New York.

INCREASING THE VITAMIN D CONTENT OF MILK. W. E. KRAUSS, R. M. BETHKE and C. F. MONROE, Ohio Agric. Exper. Stat. Bull., no. 156, 1932, p. 117.

Two lactating Holstein cows were fed from 7,500 to 200,000 rat units of vitamin D in the form of viosterol in corn oil at various periods of from twenty-one to thirty-five days' duration. The milk was tested for vitamin D by the curative or line-test procedure with rats and chicks. The vitamin D content of the milk was increased approximately in proportion to the dosage of viosterol fed to the cows. On slaughter, the cows showed no anatomic abnormalities.

KUGELMASS, New York.

A COMPARISON BETWEEN THE SPECTROPHOTOMETRIC AND BIOLOGICAL ASSAY FOR THE VITAMIN A CONTENT OF FISH-LIVER OILS. MARY A. MAGILL and WALLACE R. BRODE, Ohio. J. Sc. **33**:127, 1933.

A method for testing oils for vitamin A by the use of the antimony trichloride reagent has been applied to a number of commercial samples with some agreement between the colorimetric and biologic assay values within certain groups of samples. Differences which did occur were consistent in the samples from any one laboratory or for a given set of samples. The nature of the absorption bands produced by antimony trichloride on cod liver oils, halibut liver oils and carotene and the resulting faded bands would indicate that several closely allied compounds may be responsible for both the color reactions and the vitamin properties. Oil of peppermint contains a color-forming compound which has to a rather marked degree the same type of chromogen as is to be found in certain oils known to contain vitamin A.

KUGELMASS, New York.

PRESENT STATUS OF VITAMINS AS NUTRITIONAL FACTOR IN INFANT NUTRITION. FRANCIS T. O'DONNELL, Pennsylvania M. J. **35**:159 (Dec.) 1931.

A brief historical background of research on vitamins and a classification of the vitamins thus far identified are given. The clinical signs of deficiencies are enumerated and described for each of the vitamins. The writer points out especially that, while infinitesimal amounts of vitamins are necessary to prevent diseases caused by deficiency, a liberal supply must be provided in the diet of infants to maintain nutrition and insure optimum health.

HALL, Uniontown, Pa.

VITAMIN B DEFICIENCY: USE IN NUTRITIONAL DISORDERS. DANIEL E. BERNEY, Pennsylvania M. J. **35**:161 (Dec.) 1931.

Since investigators have determined that vitamin B is composed of two and possibly more factors, the antineuritic, heat-labile fraction, vitamin $B_1$, and the anti-

pellagric, heat-stable fraction, $B_2$, Berny believes that a revaluation of certain foods has become necessary, since some foods contain much more vitamin $B_1$ than $B_2$, and vice versa. Assuming the correctness of the conclusions of Hoobler and Outhouse and Macy, based on experiments on animals, that both breast milk and cow's milk may fail to supply the optimal amount of vitamin B, Berney presents clinical evidence of vitamin B deficiency in selected cases. He added to the diet of infants and mothers, in the case of breast-fed infants, and to the artificial food of the bottle-fed infants yeast or whole germ sugar. As a prophylactic measure, he added wheat germ sugar to the diet of both premature and very young breast-fed and bottle-fed infants, with uniformly successful results. No vitamin B deficiency became manifest in any of these infants.

HALL, Uniontown, Pa.

VARIATIONS OF GROWTH IN WEIGHT OF ELEMENTARY SCHOOL CHILDREN, 1921-1928. CARROLL E. PALMER, Pub. Health Rep. **48**:993 (Aug. 18) 1933.

The material for this study was obtained from the records of the weight, taken twice a year, of elementary school children in Hagerstown, Md., from 1921 to 1928. The purpose of the paper is to analyze the yearly fluctuations in weight and to present standards with which growth in other calendar years, particularly the recent years of economic depression, may be compared.

Two general conclusions are drawn: 1. With the exception of a few groups, the average weights of children of a given age did not vary significantly from year to year during the seven year period. 2. Average annual weight increments showed a systematic and statistically significant fluctuation during the seven year interval. The most divergent year, from May 1924 to May 1925, was found to be an inferior "growing" year, weight increments averaging approximately 92 per cent of the standards. The best "growing" year, 1926-1927, showed an average increment of more than 105 per cent of the seven year standards.

LEMASTER, Evanston, Ill.

EFFECT OF MANGANESE-DEFICIENT LETTUCE ON THE GROWTH OF RATS. J. S. MCHARGUE, Rep. Kentucky Agric. Exper. Stat., 1931, p. 24.

Lettuce seedlings were grown in sand cultures and nutrient solutions, some of which contained manganese and some of which did not. When the seedlings were grown under conditions in which they were as free from manganese as possible, the leaves contained 0.0006 per cent manganese; when they were grown in cultures and solutions containing manganese, the manganese content of the leaves was 0.1925 per cent. Rats which were fed manganese-deficient lettuce gained only 26 Gm. in eight weeks, while those which received lettuce containing manganese gained 41 Gm. on an average. In the rats which were fed manganese-deficient lettuce the hemoglobin reading was 59 per cent, as compared with 76 per cent for the rats which were fed lettuce containing manganese. Thus, manganese is necessary in the diet of the rat.

KUGELMASS, New York.

STUDY OF CALCIUM AND PHOSPHORUS ASSIMILATION BY DAIRY COWS. J. P. LAMASTER, E. C. ELTING and J. H. MITCHELL, Rep. South Carolina Agric. Exper. Stat., 1932, p. 62.

Five groups of cows at various stages of lactation were used in nineteen individual ten day mineral balance trials. In all except four cases, cows with a heavy production of milk which were fed only dry hay and grain showed slight negative balances for both calcium and phosphorus. An exceptionally high proportion of either calcium or phosphorus in the ration tends to upset the ability of the animal to assimilate these elements in the proper proportion. The negative balances of calcium and phosphorus were not due to insufficient amounts of these elements in the ration, because the amounts assimilated by the animals were less than 25 per cent of the total amount ingested. Legume hay gave the most favorable assimilation of phosphorus and calcium.

KUGELMASS, New York.

VITAMIN C POTENCY OF SPINACH UNDER VARYING CONDITIONS. EDITH PIERSON, Rep. Director, South Dakota Agric. Exper. Stat., 1932, p. 16.

The determination of vitamin C by the Hojer method cannot be recommended because of the difficulty of securing satisfactory tooth sections. Commercially canned spinach, Spinacia oleracea, contains insufficient amounts of vitamin C fully to protect guinea-pigs from scurvy when fed at the 15 Gm. level. Boiling for three minutes or allowing the opened can to stand for twenty-four hours before feeding did not significantly affect the vitamin C content. Fresh or canned New Zealand spinach gave but little protection from scurvy.

KUGELMASS, New York.

THE VITAMIN A AND THE VITAMIN E CONTENTS OF FIELD-CURED AND ARTIFICIALLY CURED ALFALFA HAY. I. L. HATHAWAY, H. P. DAVIS and R. R. GRAVES, Univ. Nebraska Agric. Exper. Stat. Research Bull., no. 62, 1932, p. 3.

A comparative study of the vitamin A content of field-cured and artificially cured alfalfa was made by comparing the growth of 124 rats which received alfalfa hay as their source of vitamin A. Artificially cured alfalfa was twice as potent in vitamin A as field-cured alfalfa. The vitamin E content of these hays was compared on the basis of the number of litters produced by groups of female rats which had received graded quantities of either field-cured or artificially cured alfalfa as their source of vitamin E. Artificial drying of alfalfa tended to preserve its vitamin E content to a greater degree than did field curing.

KUGELMASS, New York.

CLINICAL STUDY OF VITAMIN D MILK. N. E. MCBEATH and H. O. MCMAHON, Wisconsin M. J. **32**:385 (June) 1933.

Steps to prevent rickets should be begun in the prenatal period, and therefore prevention becomes the responsibility of both the obstetrician and the pediatrician.

The congenital factor is important. Because of the large number of mothers and infants who need this protection, a universal food, such as milk, which already contains the necessary calcium and phosphorus, when fortified with an increased antirachitic element, seems the ideal prophylactic. The potency of the vitamin D milk which is produced under license by certified milk producers is constantly proportionate to the amount of irradiated yeast fed to each cow; 60,000 rat units daily is needed to produce 160 rat units per quart (946.4 cc.) of milk.

A study was made in which 1 quart of vitamin D milk was given daily to twenty-five mothers during the last four months of pregnancy and to their babies for six months. A control group in which the babies were given cod liver oil between the second and sixth months was used for comparison.

Roentgen studies were made, and clinical symptoms were observed between the sixth and tenth months. In the group studied there was an incidence of rickets of 25 per cent, while in the control group the incidence was 88 per cent. The general appearance of the group which received vitamin D was much better than that of the other group, and they had no respiratory infections, while eight subjects in the control group had colds.

JANNEY, Milwaukee.

THE ALIMENTARY ABSORPTION OF WATER AND TISSUE HYDRATION IN RELATION TO DIURESIS. H. HELLER and F. H. SMIRK, J. Physiol. **76**:1 (Nov. 5) 1932.

In the guinea-pig, rabbit and rat, absorption of water from the intestine is much more rapid than its excretion through the kidney. Diuresis is decreased and the extrarenal loss of water is increased in an environment of 17 C. (62.6 F.). The authors conclude that the rate of formation of urine is not proportional to the existing degree of hydration in muscle, liver and blood.

KUGELMASS, New York.

THE SURFACE POTENTIALS OF UNIMOLECULAR FILMS OF ERGOSTEROL. RUSSEL J. FOSBINDER, Proc. Roy. Soc., London, s.A. **139**:93, 1933.

Evidence is presented to show that viosterol can be converted into vitamin D by ultraviolet irradiation. The apparatus used for the determination of the surface potential of viosterol was a quartz tray, a graduated glass scale, a Swan type of electrometer, a coated platinum air electrode and a calomel cell. The viosterol was placed on citric acid-sodium hydroxide buffers of $p_H$ 6.4. In the presence of the radiation an expansion of the film took place, indicating that the secondary alcoholic group suffers a change. Surface potential changes are plotted against time of radiation, and surface tension against area; the curves indicate the formation of vitamin D.

KUGELMASS, New York.

CHANGES IN THE BONES IN RICKETS. A. B. MARFAN, Nourrisson **21**:215 (July) 1933.

Marfan believes that the initial changes in the bones in rickets affect the marrow, thus preventing the normal formation of the osteoblasts. He thus takes issue with a recent investigator, M. Boucomont, who believes that the provisional cartilage is the first tissue to be adversely affected. Boucomont found an abundant supply of phosphatase in both rachitic bone and cartilage.

MCCLELLAND, Cleveland.

MILK ANTIBODIES IN THE SERUM OF INFANTS. P. GYORGY, E. MORO and E. WITEBSKY, Klin. Wchnschr. **10**:821 (May 2) 1931.

In forty of sixty-nine infants of average nutritional condition who were given artificial feeding, the serum contained complement-binding milk antibodies. The properties of these antibodies correspond to those of ordinary immune bodies, such as precipitins. The authors believe that albumin may be absorbed, as such, from the intestine, particularly in the case of infants. They believe that in allergy caused by milk a similar but different antibody may be concerned.

SILVERMAN, Syracuse, N. Y.

CONSTITUTIONAL FACTORS IN THE DEVELOPMENT OF NUTRITIONAL DISTURBANCE. J. C. SCHIPPERS, Monatschr. f. Kinderh. **58**:364, 1933.

The writer has been greatly influenced by the teachings of Finkelstein and quotes the text of 1924 to a considerable extent. In this discussion, Finkelstein lays great emphasis on the importance of the hydrolabile diathesis as a factor predisposing to nutritional disturbance. Schippers has reviewed his own material on 691 cases, since 1912. He shows curves demonstrating hydrolability and agrees that this is of importance, but he concludes that the hydrolability is more a result of the disturbance than the cause. The hydrolability becomes greater the longer the disturbance exists.

GERSTLEY, Chicago.

PATHOLOGY OF ALIMENTARY INTOXICATION. JOSEPH CZAPO and EDMUND KERPEL-FRONIUS, Monatschr. f. Kinderh. **59**:18, 1933.

In eight cases of alimentary intoxication, secondary chiefly to otitis media, the writers found an increased blood content of organic acid. This they ascribe to disturbance of the intermediary metabolism by bacterial toxin. Dehydration in itself is a factor in organic acidosis, in increasing the production and diminishing the elimination of acids. But dehydration is not the chief factor. Phosphates are only slightly involved in this type of acidosis, as are chlorides.

As the acidosis is due to the effect of bacterial toxins on body metabolism, administration of alkali may give some symptomatic relief, but does not strike at the cause.

GERSTLEY, Chicago.

GLYCOGEN MOBILIZATION BY SODIUM BICARBONATE. RICHARD STOHR, Ztschr. f. physiol. Chem. **217**:156, 1933.

The feeding of from 0.2 to 0.5 Gm. of sodium bicarbonate to fasting male rats caused a distinct decrease of glycogen in the liver in three hours. The glycogen in the muscles remained unchanged or else showed a slight diminution which could hardly be considered as evidence of mobilization of glycogen. The mobilization of glycogen in the liver and the consequent formation of lactic acid might be interpreted as a defensive reaction against the alkalosis which was evident from the high values of reserve. It is possible that the acid-base balance is regulated by the breakdown of carbohydrate. The decrease in glycogen in the liver by the action of alkali may be of significance in connection with glyconeogenesis from the sodium salts of organic acids.

KUGELMASS, New York.

ORAL ADMINISTRATION OF EPINEPHRINE IN VOMITING. P. BAUMRITTER and E. WILKOSZEWSKI, Pediatria polska **12**:460, 1932.

The authors use epinephrine in cases of habitual vomiting, vomiting associated with pyelitis, acute tonsillitis, meningitis serosa hydrocephalis, acute otitis media, gastro-enteritis and tuberculous meningitis. The action of epinephrine is not well known to the authors. They claim that it is possible that it produces motor inhibition of the stomach. They use a solution of 1:1,000 in distilled water, and the child receives approximately 5 drops three or four times daily.

KRUPINSKI, Chicago.

CAUSES OF VOMITING AND ITS TREATMENT IN DYSTROPHY. B. J. WISNIEWSKI, Pediatria polska **12**:466, 1932.

The author reports a series of cases of dystrophic, undernourished infants in which the history and physical examination revealed nothing abnormal except that the formula was very low in caloric value. All of the children were placed on either whole cow's milk or evaporated milk with the addition of about from 15 to 18 per cent of sugar. All got well in a short time. KRUPINSKI, Chicago.

GROWTH AND THE CAROTENOIDS. HANS V. EULER and ERIKA KLUSSMAN, Ark. kemi, min. geol. **10**:1, 1932.

The authors attempted to determine the change in weight of experimental rats that were given doses of vitamin A and injections of thyroxine simultaneously. Thirteen rats were given the usual basal diet containing also vitamins B, C and D. Nine of these rats were given daily doses of carotene, and thyroxine was injected daily into seven of the latter. The rats which were given carotene and thyroxine gained about 1 Gm. per day; those which were given thyroxine but no carotene lost about 9 Gm. per day, and those which were given carotene without thyroxine gained about 11 Gm. daily. An equilibrium is reached during the simultaneous administration of thyroxine and carotene (vitamin A) when the loss of weight due to thyroxine is compensated by the intake of carotene.

KUGELMASS, New York.

INFLUENCE OF RELATIVE VITAMIN VALUE OF MILK ON GROWTH, DIGESTION AND NITROGEN AND MINERAL METABOLISM IN CALVES. E. G. SVESHNIKOVA, Zap. Leningrad Selsk. Khoz. Inst. **7**:120, 1929.

While the addition of cod liver oil to the ration of a dairy cow increases the vitamin D content of the milk, it reduces the fat content and is not a profitable practice, because of the depressing effect it has on the utilization of the fat content of the feed. The milk of a cow fed a ration rich in vitamins produced average daily gains of 1.25 Gm. in a rat which was fed 5 cc. of her milk daily, while milk from a cow on a ration poor in vitamins fed at the same rate produced

gains of only 0.69 Gm. daily. When the milk from the cows was fed to suckling calves, the vitamin content had no effect on the rate of digestion or on the nitrogen and mineral metabolism of the animals. The milk enriched with vitamin D produced no better growth in calves than ordinary milk.

KUGELMASS, New York.

THE VARIABILITY OF THE NEED OF THE VITAMIN B COMPLEX. A. DEVRIES and G. J. PUISTER, Arch. néerl. de physiol. **18**:71, 1933.

A large proportion of cod liver oil (15 per cent) with the normal minimum of dried yeast in the diet delays growth and causes loss of hair, especially of the abdomen. A higher proportion of yeast (12 per cent) prevents or cures the symptoms of the action of cod liver oil (balancing effect). Vitamin $B_2$ appeared to be the effective element in yeast, while vitamin $B_1$ (activated acid clay) did not show a balancing effect in proportion to cod liver oil. KUGELMASS, New York.

DEPRESSED GASTRIC SECRETORY ACTIVITY. S. LINDGREN, Acta med. Scandinav., supp. 48, 1932, p. 235.

An investigation of the depressed activity of gastric secretion among the population of the Vasterbotten province of northern Sweden has been made; it showed a large proportion of persons with a negative reaction to congo red. Of the various causes for this defective activity of the gastric secretions the poor condition of the teeth may be a contributing cause. No relation was found to the use of alcohol or tobacco. The inhabitants were classified according to the nature of their dietary into three groups: (1) a diet of cereal flour and milk, prevalent along the coast; (2) a diet containing pork, among the inhabitants of the forest region, and (3) a mixed diet. The low gastric acidities were especially common among the first group. This condition is not attributed to a deficiency of vitamin C but is regarded as a physiologic adaptation to a dietary requiring less free hydrochloric acid than a diet of meat does. However, this secondarily reduces the capacity to resist factors inducing gastritis caused by inactivity.

KUGELMASS, New York.

CAROTENOIDS AND VITAMIN A IN ANIMAL AND PLANT TISSUES. H. V. EULER, ULLA GARD and H. HELLSTROM, Svenska kem. tidskr. **44**:191, 1932.

Spectroscopic bands were recorded for preparations from the procreative tissues of fish, mammals and plants. Carotene was demonstrated in all of these; the quantities were very minute, however, in some specimens, e. g., lily stamen and pike milt. The universal presence of carotene in these tissues suggests that it is an essential factor in growth. Other tissues, sites of cell proliferation, also contain this pigment, but bone marrow, which was positive for vitamin A, gave no carotene band. Xanthophyll and zeaxanthin bands occurred sporadically, and chlorophyll was present in the roe of fresh-water fish. KUGELMASS, New York.

## Prenatal Conditions

FOETAL BLOOD STUDIES: IV. THE OXYGEN AND CARBON-DIOXIDE DISSOCIATION CURVES OF FOETAL BLOOD. N. J. EASTMAN, E. M. K. GEILING and A. M. DELAWDER, Bull. Johns Hopkins Hosp. **53**:246 (Nov.) 1933.

At gas tensions between 25 and 60 mm. of mercury fetal blood absorbs oxygen more effectively than the blood of the mother. At all gas tensions fetal blood releases carbon dioxide more readily than the blood of the mother. These two adjustments facilitate the placental interchange of these gases, but result in a low oxygen tension in fetal tissues and a high partial pressure of carbon dioxide. At the moment respiration begins at birth the carbon dioxide tension of the blood

of the umbilical vein varies within wide limits, a circumstance which suggests that some factor other than the carbon dioxide tension of fetal blood is the dominant one in initiating this phenomenon. AUTHORS' CONCLUSIONS.

HEREDITARY ARTHRODYSPLASIA ASSOCIATED WITH HEREDITARY DYSTROPHY OF THE NAILS. J. W. TURNER, J. A. M. A. **100**:882 (March 25) 1933.

Attention is called to a hereditary arthrodysplasia which in thirty-five of seventy-nine persons in two families was always associated with dystrophy of the nails. As the name signifies, underdevelopment of the joints is the characteristic finding. This may cause limitation of motion. The typical dystrophic nail is small and thin, disappearing about half-way down the nail bed. The fleshy end of the finger turns back over the nail, rendering the finger useless for picking up thin objects.

BONAR, Salt Lake City.

CONGENITAL HEART BLOCK. W. M. YATER, J. A. LYON and P. E. MCNABB, J. A. M. A. **100**:1831 (June 10) 1933.

Including the authors' report of a case of congenital heart block in an infant aged 2 months, forty-four acceptable cases have been reported. In five cases autopsies were performed. In only three were histologic studies made of the conduction system. In most of the cases the cause appears to have been a congenital defect in the bundle of His. The most common clinical diagnosis was defect of the interventricular septum, and in the case reported such a defect occurred together with nearly complete congenital absence of the budle of His.

BONAR, Salt Lake City.

CONGENITAL AIR CYST OF THE LUNG. C. V. CROSWELL and J. KING, J. A. M. A. **101**:832 (Sept. 9) 1933.

A case of solitary congenital air cyst (balloon cyst) of the left lung is reported. The child's condition varied from that of threatened asphyxia to that of restful normal breathing following aspiration of from 8,000 to 10,000 cc. of air from the sac every four hours. Iodized poppy seed oil was injected into the cavity for diagnostic purposes. The patient was deemed too ill for a resort to surgery. By the end of the week improvement was noted, aspiration yielding only 500 cc. of air. Progressive improvement has followed, and a hopeful but guarded prognosis seems justified. The question is asked: "To what particular therapeutic measure, if any, is the patient indebted?"

BONAR, Salt Lake City.

FAMILIAL CONGENITAL DISLOCATION OF THE HIP. S. S. HANFLIG, New England J. Med. **209**:544 (Sept. 14) 1933.

Two theories of pathogenesis are suggested: (1) that the dislocation is the result of chronic trauma to which the lower limbs and consequently the joints of the hips are exposed in the second half of prenatal life; and (2) that the dislocation is induced by atypical morphologic conditions which can be transmitted from one generation to the next. In an Irish family five of the twelve children had congenitally dislocated hips. In two of these the dislocation was unilateral; in the remaining three it was bilateral. Both parents had normal hips. Five of the twelve children had normal hips. There were no data on the remaining two. None of the children who had congenitally dislocated hips had borne children. The only occurrence of the deformity in the second generation was in L., a daughter of John, whose hips were normal.

GENGENBACH, Denver.

POSTMATURITY AND MALFORMATION OF THE FETUS. PERCY MALPAS, J. Obst. & Gynaec. Brit. Emp. **40**:1046 (Oct.) 1933.

In analyzing a series of 238 cases of fetal malformations occurring from 1923 to 1932 at the Liverpool Maternity Hospital, Malpas observes a relation between certain types of malformations of the fetus and postmaturity. He bases his criteria of postmaturity on the continuance of pregnancy for at least two weeks beyond term, on anatomic and roentgenologic evidence, on absence of changes due to maceration and on persistence of fetal heart sounds and movements to within a few days of delivery.

Postmaturity occurred in only 21 instances, namely, 9 cases of anencephaly, 10 cases of hydrocephalus and spina bifida, either separated or combined, 1 case of webbed fingers and 1 case of talipes. This reveals that postmaturity is not a feature of fetal malformation in general, but rather of malformation of the brain and spinal cord. The glandular system is also defective, particularly the suprarenal bodies and the pituitary glands, which may even be absent. He believes that the onset of labor is determined by the optimum viability of the fetus, and that possibly the suprarenal glands, the pituitary gland or the nervous system or all of them are the tissues that take part in the stimulation of the expulsive mechanism of the uterine neuromuscular system when gestation is at term.

ADAIR and TESAURO, Chicago.

CONGENITAL UMBILICAL HERNIA. REPORT OF A CASE OF AMNIOTIC HERNIA. EDGAR FRESHMAN, Lancet **2**:701 (Sept. 23) 1933.

A male infant was seen about two hours after delivery. The abdominal wall had failed to develop, so that the abdominal contents, protruding as a large hernia, were visible through a transparent covering. The child was operated on immediately, and left the hospital at the age of 1 month, progressing well thereafter. When operation is deferred for any length of time, the two main dangers are paralytic ileus and infection of the wall of the sac. Injury during delivery may render the case hopeless.

LANGMANN, New York.

CONDITIONS OF FOETAL RESPIRATION. J. BARCROFT, Lancet **2**:1021 (Nov. 4) 1933.

In the course of studies by Rothschild (1932) and Herkel, Hill and Barcroft (1933) it was found that as pregnancy proceeded in the rabbit the blood leaving the uterus and returning to the mother became increasingly dark. It was also found that during the latter part of pregnancy the blood of the fetus was richer in base than that of the mother. Barcroft's experiments were performed on a series of goats all "stocked" about the same time. One goat was operated on each week, starting at the end of the seventh week of gestation. These studies lead him to state that: "It seems to be proved: (1) with regard to the mother, (*a*) that from about the middle of pregnancy onward, the dissociation curve shifts to the right and (*b*) that the shift may be accounted for by an increase in the hydrogen-ion concentration of the maternal blood; (2) with regard to the foetus (*a*) that, on the whole, from about the same time, the dissociation curve of the foetal blood at the relevant pressures of oxygen falls to the left of the normal position, and (*b*) that the shift is not due to abnormal alkalinity of the foetal blood, for this is no more alkaline than that of the normal goat; (3) that the characteristic curve of foetal blood is due to a specific form of haemoglobin."

LANGMANN, New York.

URETERAL STENOSIS. DUNCAN M. MORISON, Tr. Edinburgh Med.-Chir. Soc., 1933, p. 168; in Edinburgh M. J., Sept. 1933.

Morison presented two cases of unilateral stasis of the upper part of the urinary tract caused by stenosis of the ureter. In one of the cases scarlet fever at the age of 8 years precipitated a recurrence of the hematuria and lumbar pain.

On roentgen examination a small calculus was found in the renal pelvis, with advanced hydronephrosis on the same side. Treatment consisted in dilation and catheterization; the contents were found to be infected with colonic organisms. Good drainage was provided after further dilation, and the function of the kidney improved to two-thirds that of the normal side. The cause of the condition was the narrowing at the junction of the pelvis and ureter, and this was found to be corrected after the removal of the calculus. The conservative treatment produced satisfactory recovery and function.

A child, aged 5 years, suffering from persistent nocturnal enuresis, was found to have marked hydronephrosis on the left side, without infection. Dilation of the ureter was indicated. Retrograde pyelographic studies showed dramatically the process of the tubular absorption. NEFF, Kansas City, Mo.

NEW METHOD FOR PREVENTING ASPHYXIA OF THE FETUS IN PROLONGED OR DIFFICULT LABOR. D. THÉODORIDÈS, Bull. Soc. d'obst. et de gynéc. **22**:603 (July) 1933.

During labor there are two principal factors which produce an increase of carbon dioxide in the maternal blood: (1) the muscular efforts of labor and (2) the periodic arrest of the respirations of the mother. In prolonged and difficult labor this increase in carbon dioxide may react on the infant to produce asphyxia. The author recommends two methods of combating this. The first is by the injection of lobeline, which he accepts as a specific stimulant of the respiratory center, causing deeper and more rapid respirations. A first dose of 0.003 mg. is given and subsequent doses are gradually increased, if necessary, to 0.009 mg. The second method of preventing fetal asphyxia is by the administration of ozone to the mother. If ozone is not available, oxygen may be used instead. Lobeline and ozone or oxygen may be used together to advantage, the latter tending to act as an antidote to an overdose of the former. The author states that he used these methods in sixteen cases of difficult labor, with only one fetal death, which was due to intracranial hemorrhage. He considers that this represents a marked reduction in the mortality in such cases. GLASER, Rochester, N. Y.

CONGENITAL DISEASE OF THE HEART. LOUIS U. RABUFETTI and E. BRAUN MENENDEZ, Arch. méd. d. Hop. Ramos Mejia **15**:71 (March) 1933.

Those who study congenital abnormalities of the heart find it difficult to make an exact diagnosis of the underlying lesion. Even after the electrocardiogram, roentgenogram and other modern means have been used in reaching the clinical diagnosis, the pathologist often finds that this diagnosis was wrong. Perusal of the literature reveals contradictory statements regarding the subject. A good differential diagnosis is presented, along with the clinical, roentgenographic and electrocardiographic observations. One case is reported.

HERRON, Spokane, Wash.

TWO CASES OF CONGENITAL MICROMELIA. B. V. BAPTISTA, Arch. de pediat. d. Rio de Janeiro **5**:349 (Aug.) 1933.

Baptista gives the history, physical findings, pictures and roentgenograms in two cases of achondroplasia. One patient was male and the other female.

SANFORD, Chicago.

FAMILIAL OCCURRENCE OF PSEUDOHERMAPHRODITISM. KARL RUPILIUS, Arch. f. Kinderh. **100**:206 (Oct. 31) 1933.

Two of six children in a family exhibited pseudohermaphroditism. The parents and four of the children were normal. There was no history of congenital anomalies in either the father's or the mother's family. Both infants with pseudohermaphroditism were christened as boys and were thought to have hypospadia. Intercurrent infections caused the death of both infants, and autopsy showed a uterus and two ovaries in each of them. LEMASTER, Evanston, Ill.

FAMILIAL SYNDACTYLISM. JAROSLAV CIPEK, Časop. lék. česk. **71**:806 (June 24) 1932.

The literature is reviewed, and three cases are cited in detail. These are of a grandmother, father and daughter of 78, 40 and 5 years of age, respectively. No other member of the three generations has a deformity similar to syndactylism or polydactylism. Roentgenograms and photographs are given. A combination of syndactylism and polydactylism was found in the three patients. In discussing the question of heredity, the work on chickens with hereditary polydactylism is cited. It is found that the supernumerary digits develop before the regular digits in the embryologic sequence, and Tobiasek states that the deformity is usually passed from mother to son and from father to daughter. STULIK, Chicago.

BILATERAL AMASTIA WITH ASSOCIATED DEFORMITY OF THE EXTREMITIES. JAROSLAV GLOS, Časop. lék. česk. **71**:865 (July 8) 1932.

A woman of 27 years, born with neither breasts nor nipples, had four digits on the right hand and the right foot. She gave birth to a normal child which was fed artificially. The child is now 8 years of age. During pregnancy no reaction took place in the chest. STULIK, Chicago.

EXPERIMENTAL PATHOGENESIS OF CYCLOPIA. N. BLATT, Miscarea med. **6**:52, 1933.

Cyclopia means that the anterior end of the brain, owing to a developmental defect, hinders both optic anlagen from being located on the lateral faces of the vesicles of the brain, so that both come to lie side by side and fuse together into one eye of normal external aspect. As a matter of fact, cyclopia is really a double eye.

The existence in these eyes of a single choroid and a single sclerotic in addition to two retinas argues for cyclopia being due to the approach to each other and fusion of two eyes the developmental time of which is likely to fall in the neurula stage, at which the optic cup is already developed, and the retina fully formed, but the choroid and sclerotic are still absent.

The factors deemed causative of cyclopia are as follows: psychic influences on the part of the parents, local inflammation in the region of the eyes, abnormal chemical influences on the embryo, malnutrition of the growing germ, faulty temperature, pressure of the fetal membranes on the embryo and diseases of the uterus.

The results of experiments done on amphibian embryos with a view to produce cyclopia in adult animals are also adapted to solve the phylogenetic problems connected with cases of human cyclopia.

Since a more advanced gastrula or an earlier neurula stage allows the optic anlagen to be easily recognized by two strongly pigmented areas situated on both sides of the neural plate, benefit can be derived from this knowledge by conducting the experiments on amphibian embryos just at those stages. If the median portion of the neural plate is exposed to any deleterious action leading to retardation of development or destruction, or cut off in an experimental way, the optic plates, i. e., the eye-forming regions in the medullary plate, come up to one another, thus giving rise to the formation of the cyclopean monstrosity. Strong evidence seems to prove that the developmental mechanism concerned is the same, e. g., the malformations of human embryos due to pressure by amniotic bands.

For the most part, amphibians (salamanders and Triton taeniatus, alpestris and cristatus) were used for the experiments. These animals are best fitted for such biologic tests as they are oviparous and are endowed with high powers of resistance and of regeneration, too, especially as to the eyes.

These experimental interferences can result in the postoperative genesis of a quasi-unit of an eye with a monocentric crystalline lens in the embryo 10 days old.

The experiments should, however, be carried out on very young embryos, viz., within the first fifteen hours of development. At the germ cell stage, however, at which the determination of the single embryonic cells has not yet taken place, operation ought not to be done, because the experimental production of cyclopia would prove a failure. In the more advanced stage of development, beyond the neurula stage, when the germ, already determined, is highly differentiated, the operation—though in very rare cases—can prove successful and thus produce cyclopean defects.

A second plausible explanation of the genesis of human cyclopia is offered by the lesions the embryos are frequently exposed to by the pressure of amniotic bands. If an amniotic band exerts an abnormal pressure on the head end of the embryo, there exists the possibility of a cyclopia developing.

Cyclopia can be regarded only as the product of an extensive deficiency involving the embryonic cephalic end and stretching as far as the optic anlagen and even beyond.

N. BLATT. [ARCH. OPHTH.]

MEGADUODENUM IN INFANTS, CAUSED BY CONGENITAL ATRESIA AND STENOSIS. R. J. HARRENSTEIN, Maandschr. v. kindergeneesk. **2**:475 (July) 1933.

The diagnosis of duodenal obstruction above Vater's papilla may give rise to difficulties. Roentgen investigation may be useful. When there is a duodenal obstruction, the part of the duodenum above the place of obstruction becomes much dilated. The megaduodenum is found at roentgen examination and also at operation or at autopsy. Different factors play a rôle in the origin of duodenal occlusion during embryonal and fetal development or after birth. In 30 per cent of cases of congenital occlusion of the intestinal tract the occlusion occurs in the duodenum. Harrenstein reports seven cases of congenital megaduodenum caused by atresia or stenosis of the duodenum. In all the cases bile was present in the vomitus, which made the diagnosis easier. Four patients died after the operation. In only one case was the obstruction caused by a compressing band.

VAN CREVELD, Amsterdam, the Netherlands.

CONGENITAL ATRESIA OF THE DUODENUM. W. E. JAK, Nederl. tijdschr. v. geneesk. **77**:2683 (June 10) 1933.

A case of marked distention of the duodenum in a new-born infant is described. Operation revealed what was apparently congenital atresia with torsion.

VAN CREVELD, Amsterdam, the Netherlands.

## Diseases of the New-Born

PURULENT PAROTITIS IN THE NEW-BORN. THEODORE O. ELTERICH, J. Pediat. **3**:761 (Nov.) 1933.

A case of purulent parotitis in an infant, 14 days old, is reported, with a discussion of the literature on this subject. There were fever and enlargement of the parotid gland. Pus containing Staphylococcus aureus could be expressed from Stenson's duct. Hot boric acid dressings were applied and complete recovery occurred in a few days without surgical intervention.

LEMASTER, Evanston, Ill.

CARDIOSPASM AND OTHER OBSTRUCTIONS OF THE UPPER GASTRO-INTESTINAL TRACT IN THE NEW-BORN. J. AIKMAN, New York State J. Med. **33**:865 (July 15) 1933.

Aikman reviews briefly the causes of vomiting of the new-born, and discusses the methods of diagnosis and treatment of vomiting which has its origin in the upper part of the gastro-intestinal tract. The discussion of cardiospasm is particu-

larly complete, with five cases reported in detail. Characteristically, vomiting in this condition dates from the first attempts at feeding and the vomitus contains little or no gastric juice. Cardiospasm probably occurs more frequently than most pediatricians realize and would be more often diagnosed if roentgen studies were more generally employed in cases of vomiting of unknown origin during the early days of life.

GLASER, Rochester, N. Y.

THE CAPUT SUCCEDANEUM: A HINDRANCE TO LABOUR. JAMES ROBERT GOODALL, J. Obst. & Gynaec. Brit. Emp. **40**:1021 (Oct.) 1933.

The author believes that the caput succedaneum has a passive rôle in the first stage of labor, and does not act as a dilator of the cervix as is commonly believed. During the second stage the caput becomes an actual hindrance to labor, because, owing to its usual eccentric position over the fetal head, the bulk of the fetal head is thrown out of the axis of the pelvis. As a result of the eccentricity, if uterine contractions are not sufficiently strong to push the presenting caput out of the axis of the vagina and pelvis, rotation will be arrested and labor prolonged.

ADAIR and TESAURO, Chicago.

EXOMPHALOS. GERTRUDE HERZFELD, Tr. Edinburgh Med.-Chir. Soc., 1933, p. 171; in Edinburgh M. J., Sept. 1933.

Herzfeld operated on an infant 4 hours old for exomphalos. When freeing the adhesions of the cecum and ileum to the sac, she found it necessary to implant the lower portion of the ileum into the transverse colon and to resect the ileocecal region. In spite of the desperate postoperative appearance of the infant it recovered and was presented at the surgical society meeting; apparently it was a perfectly normal infant, 8 months of age.

NEFF, Kansas City, Mo.

CAUSES OF STILLBIRTHS IN THE CITY OF TOULOUSE DURING THE PAST TEN YEARS. AUDEBERT and BOURREL, Bull. Soc. d'obst. et de gynéc. **22**:719 (Oct.) 1933.

Less than one third of the infants born in the city of Toulouse are delivered in hospitals. The average incidence of stillbirths for the city during a period of ten years was 4.1 per cent; that for the hospitals was 6.96 per cent. The difficult cases naturally gravitate to the hospitals. Of 4,264 infants delivered in hospitals during the period of ten years, 296, or 6.96 per cent, were stillborn. The outstanding causes were: syphilis, 9.7 per cent; toxemia of pregnancy, 15.5 per cent; prematurity, 15.2 per cent; malpresentations or difficult labors, 19.8 per cent. Thus, 60.2 per cent of the stillbirths were due to the aforementioned causes, which the authors regard as largely preventable. The most important factors in prevention are proper antepartum care of the mother, with insistence on periodic methodical observation by an obstetrician, and assurance that women in labor shall receive the best of obstetric care.

GLASER, Rochester, N. Y.

BIOMETRIC DATA ON THE NEW-BORN IN GROSSETO. BENEDETTO DE LUCA, Pediatria **41**:1382 (Nov.) 1933.

De Luca undertook to determine the average weights and heights of infants born in the maternity department of the Grosseto Hospital, with a view of determining whether these figures paralleled those of the new-born in other parts of Italy.

His studies and observations included 305 new-born infants, of which 158 were boys and 147 girls. Detailed figures are given in relation to the new-born infants of primiparas and multiparas. The infants studied represented the poorer elements of the population. He contends that a study covering the new-born infants of

the entire population would result in figures relatively higher than those resulting from the study of this group.

The summarized results are as follows:

| | Average Weight, Gm. | Average Height, Cm. |
|---|---|---|
| 158 new-born boys..... | 3,645 | 50.7 |
| 147 new-born girls..... | 3,422 | 50.0 |
| 305 new-born boys and girls..... | 3,533 | 50.35 |

De Luca directs attention to the fact that the heights are relatively lower and the weights relatively higher than the averages generally found, and explains this by the assertion that the infants in his series were more robust than the average.

SIGNORELLI, New Orleans.

THE ISLAND TISSUE OF A NEWLY BORN CHILD OF A MOTHER WITH DIABETES. K. A. HEIBERG, Virchows Arch. f. path. Anat. **287**:628, 1933.

A mother who had a stillborn child three years previously, and who was suffering from severe diabetes (requiring from 40 to 60 units of insulin a day), gave birth to a child weighing 3.65 Kg. At birth the child's blood sugar was 88 mg. per hundred cubic centimeters (the method is not given) which decreased to 70 mg., increased for a short time after administration of a dextrose solution and remained between 60 and 70 mg. The child died on the second day of life. Heiberg counted the islands of Langerhans and found no increase or only a very slight increase as compared with the number in normal infants. The weight of the pancreas was three times as great as that of a normal infant (5 Gm. as compared with from 1.4 to 1.5 Gm.). Therefore it seems that the number of islands should have been greatly increased. The author gives his measurements of the diameter of the islands at different ages as compared with those of other authors and stresses the importance of the objective evaluation of the function of the islands which he has stressed for twenty years. SCHOENTHAL, New York.

EREPSIN IN LIQUOR AMNII AND FETAL INTESTINES IN EVERY STAGE OF PREGNANCY AND IN MECONIUM OF HUMAN NEW-BORN. M. ABE, Jap. J. Obst. & Gynec. **16**:225 (June) 1933.

Abe's experiments show that the optimal concentration of the hydrogen ions of erepsin in human liquor amnii is from $p_H$ 7 to 8, and more often $p_H$ 8. He has found erepsin in human amniotic fluid during the tenth month of pregnancy, and more abundantly in fluids mixed in the meconium. He has demonstrated the presence of erepsin in the amniotic fluid from the second to the seventh month of pregnancy, and the fact that in the second month the function of the human fetal intestines could not be proved leads to the conclusion that erepsin was originally contained in the liquor amnii. He has also found erepsin in the fetal intestines in the third month; its action at this stage is rather weak and increases with each successive month of pregnancy. The action of erepsin seems to be more intense in the mucosa than in the muscular layers of the intestines. But during fetal life the local differences of the intestines were not remarkable. Finally, the author has demonstrated erepsin in the meconium of the human new-born.

ADAIR and TESAURO, Chicago.

ICTERUS GRAVIS FAMILIARIS OF THE NEW-BORN. H. FUJIMORI, Jap. J. Obst. & Gynec. **16**:234 (June) 1933.

Fujimori reports a typical case of icterus gravis familiaris of the new-born, the only case, according to his investigation of the literature, reported in Japan. He calls attention to the fact that the mother, a septipara, had been married twice, and that the offspring of the first marriage had only mild jaundice, while the first four babies born from the second marriage died of severe jaundice on the

fifth and sixth days after birth. The case reported was the result of the seventh pregnancy. Icterus started on the second day and on the fifth became so severe that the life of the infant was in danger. Active treatment with maternal blood injected into the gluteal muscles, dextrose, insulin and water saved the infant. The reactions to tests for syphilis were negative. The hemoglobin dropped from 102 per cent of normal on the fourth day to 66 per cent on the eighth day. The red cell count decreased from 4,730,000 on the fourth day to 3,700,000 on the eighth day, and on this day the cells were nucleated and of irregular size and shape.

Fujimori believes that the icterus was due to the destruction of erythrocytes. Futhermore, since severe jaundice developed only in the children from the second marriage, he thinks that constitution plays a great part in the explanation of icterus. Also, since this is the only case reported in Japan, he says that colored races show a resistance against abnormal development of pigments in the skin as in severe jaundice.

ADAIR and TESAURO, Chicago.

MUTUAL RELATION BETWEEN THE HEIGHT AND WEIGHT OF THE JAPANESE NEW-BORN. K. OKADA, Jap. J. Obst. & Gynec. **16**:242 (June) 1933.

During the last six years this relation has been studied at the Municipal Lying-in Hospital of Osaka, by investigating 11,068 new-born infants, all delivered in not less than two hundred and fifty-three days from the first day of the last menstruation. The results show a mutual relation between the height and the weight of the new-born: The baby's weight increases with its increase in height.

ADAIR and TESAURO, Chicago.

PEMPHIGUS NEONATORUM AND CONSTITUTION. B. P. B. PLANTENGA Maandschr. v. kindergeneesk. **2**:407 (June) 1933.

Plantenga is of the opinion that often pemphigus neonatorum which does not react soon to good treatment and care is caused by constitutional sensitiveness to animal fat. The consequences of this conception for the treatment of pemphigus neonatorum are stressed.

VAN CREVELD, Amsterdam, the Netherlands.

CEREBRAL DEVIATIONS IN THE NEW-BORN. A. F. A. S. VAN WESTRIENEN, Maandschr. v. kindergeneesk. **2**:502 (July) 1933.

In a general survey van Westrienen mentions the newer conceptions of the significance of trauma at birth as the explanation of different neurologic deviations arising directly or shortly after birth and discusses the extent to which this explanation may hold true for several conditions.

VAN CREVELD, Amsterdam, the Netherlands.

## Acute Infections

THE ADDIS SEDIMENT COUNT IN NORMAL CHILDREN; THE ADDIS SEDIMENT COUNT IN SCARLET FEVER. JOHN D. LYTTLE, J. Clin. Investigation **12**:87 and 95 (Jan.) 1933.

The technic of Addis for the quantitative determination of the excretion of protein, casts and cells in the urine was applied to normal children, aged from 4 to 12 years. An aliquot (10 cc.) of a twelve hour night specimen was centrifugated, the supernatant fluid removed to a measured volume, and the sediment mixed with the remaining fluid by means of a capillary pipet. The casts and cells were then counted in a drop transferred to a hemocytometer. Tentative

standards were set up for normal children of this age group, as shown in the accompanying table:

*Upper Limit of Normal Excretion Per Twelve hours in Children from 4 to 12 Years of Age*

| | |
|---|---|
| Protein | 35 mg. |
| Casts | 10,000 |
| Red blood cells | 600,000 |
| Epithelial and white blood cells | 600,000 (male) / 1,000,000 (female) |

The technic described was applied in fourteen cases of scarlet fever. All of the patients showed moderate transient increases in the excretion of protein and formed elements during the period from eight to forty-five days after the onset of scarlet fever.

GUEST, Cincinnati.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES—APRIL 23-MAY 20, 1933. Pub. Health Rep. **48**:637 (June 9) 1933.

For the country as a whole the year 1933 continued to maintain a record-breaking low incidence of diphtheria. The number of cases of influenza, poliomyelitis and meningococcic meningitis was slightly less than during the corresponding period in recent years. The incidence of smallpox was at an unusually low level.

For the whole reporting area the incidence of measles was less than that of the three preceding years but about 10 per cent above the incidence in 1929. Scarlet fever showed a 10 per cent decrease as compared to the figures for 1932. Cases of typhoid fever remained at about the usual number.

The average mortality in large cities for this four week period was 11 per thousand of population, definitely lower than in recent years.

LEMASTER, Evanston, Ill.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES—MAY 21-JUNE 17, 1933. Pub. Health Rep. **48**:787 (July 7) 1933.

An increase in the incidence of typhoid fever was noted in all sections of the country except in the Rocky Mountain and Pacific Coast areas. The incidence of measles, diphtheria, smallpox, scarlet fever, poliomyelitis and influenza was considerably lower than that for the corresponding four week period in recent years. The number of cases of epidemic meningitis was less than usual in all states except Illinois.

LEMASTER, Evanston, Ill.

OBSERVATIONS ON DYSENTERY IN CHILDREN. DAVID NABARRB and A. GORDON SIGNY, Arch. Dis. Childhood **7**:327 (Dec.) 1932.

The authors give the incidence of dysentery from Flexner and Sonne bacilli in a children's hospital, totaling 106 cases over a period of four years. There were 87 cases of dysentery due to Sonne bacilli, 18 due to Flexner Z bacilli and 1 due to Flexner W bacilli. Death occurred in 4.5 per cent of the cases of infection due to Sonne bacilli, and in 10.5 per cent of those of infection due to Flexner bacilli.

The bacteriology of the feces and the agglutination of the blood are discussed, and suggestions are given for minimizing the risk of spreading the infection in institutions.

KELLY, Milwaukee.

THE ASPIRATION TREATMENT OF LARYNGEAL DIPHTHERIA. OLGA F. TREGELLES, Brit. J. Child. Dis. **30**:97 (April-June) 1933.

Every patient with croup showing definite signs of obstruction was examined with a modified, child's size Chevalier Jackson laryngoscope. "In cases where the airway is good and the true cords can be easily seen, and where obstruction appears

to be due to loose pieces of membrane, aspiration is generally enough. Where the whole glottis is swollen and edematous, and where the false cords are so swollen that the true cords can hardly be seen, aspiration is unlikely to improve matters and intubation is most efficacious."

A second aspiration from four to six hours after the administration of antitoxin was often found effective in removing large pieces of membrane and relieving the obstruction.

The intravenous administration of antitoxin is not looked on with much favor in cases of acute laryngeal diphtheria because of the frequent occurrence of serum shock and its attendant respiratory difficulty.

Although the series of cases reported here is small, the author feels that her experience substantiates that of American workers in showing that the incidence of operation for laryngeal diphtheria is less if aspiration is performed and that the death rate following operation is lower. LANGMANN, New York.

EXTENSIVE PURPURA SIMPLEX FOLLOWING MEASLES. L. J. M. LAURENT, Brit. J. Child. Dis. **30**:104 (April-June) 1933.

A boy, aged 8 months, had purpuric spots on the cheeks on the twentieth day after a mild attack of measles which subsided apparently without complications. In the course of the next two days the spots increased rapidly in size and large fresh areas of purpura appeared on the nose, ears, forearms and thighs. The temperature ranged between 99 and 103 F. There was no hemorrhage from the gums, mouth, nose, bowels or urethra.

Twenty-four hours after the intramuscular injection of 50 cc. of the mother's blood the lesions ceased to extend, and no new ones appeared; at the end of six days the cutaneous manifestations had entirely cleared.

A blood count made before the injection of whole blood showed: hemoglobin, 45 per cent; red cells, 4,200,000; white cells, 12,400; polymorphonuclears, 22 per cent; large mononuclears, 10 per cent; lymphocytes, 68 per cent, and platelets, 220,000.

This case was thought worthy of report for two reasons: (1) the comparative rarity of purpura following measles and (2) the absence of thrombocytopenia in spite of the extensive purpuric lesions. LANGMANN, New York.

A CASE OF RUBELLA COMPLICATED BY PURPURA HAEMORRHAGICA. WILLIAM GUNN, Brit. J. Child. Dis. **30**:111 (April-June) 1933.

A girl of 9½ years was admitted to the hospital with the history of having had a headache two days before and having presented a rash on the face and chest the day before. She presented a generalized macular rash, in places somewhat irregular and blotchy. The temperature was 100 F. On the second day the rash had definitely faded, but about a dozen minute petechiae were noted in both supraclavicular fossae and in the antecubital fossae as well. The bleeding time was five and one-half minutes. The girl then had a severe attack of epistaxis. On the third day a fresh crop of petechiae appeared above both clavicles. Forty cubic centimeters of horse serum was given intramuscularly without apparent benefit.

On the fourth day fresh crops of petechiae appeared over the upper end of the sternum and on the flexor surfaces of both forearms. Twenty cubic centimeters of a hemostatic preparation was injected intramuscularly, and a few hours later 50 cc. of the mother's whole blood.

The blood platelet count was 61,800 several days after the intramuscular injection of blood (there is no earlier report). It rose to 214,000 in the course of about two weeks. LANGMANN, New York.

A Case of Scarlet Fever Followed by Meningeal Haemorrhage. E. W. Goodall, Brit. J. Child. Dis. **30**:117 (April-June) 1933.

A boy, aged 9 years, was admitted to the hospital on the fourth day of a mild attack of scarlet fever. The following day the temperature was normal, and the tonsils, which had been swollen and covered with whitish exudate, cleared rapidly. About twenty-seven days later, the convalescence having been normal, he complained of headache and was kept in bed although there was no fever. The headache persisted; two days later he vomited and twitching of the arms and eyelids, as well as nystagmus, was noticed. Later generalized convulsions set in. On lumbar puncture, 45 cc. of clear fluid under considerably increased pressure was obtained. (The fluid was not examined bacteriologically or microscopically.)

At autopsy an extensive subdural hemorrhage was found on the left side, extending in front of and behind the fissure of Rolando, and there was slight hemorrhage in a similar position on the other side. There were two small hemorrhagic spots on the epicardium and two in the aorta. Langmann, New York.

Scarlatiniform Dermatitis After Injection of Toxoid-Antitoxin. George Chesney, Brit. M. J. **2**:98 (July 15) 1933.

The author reports a troublesome exfoliating dermatitis occurring in a girl, aged 16, following two injections of 1 cc. each of a toxoid-antitoxin mixture given within a period of seven days. The dermatitis was due possibly to an acute sensitivity to the serum. Royster, University, Va.

Encephalitis Following Vaccination: With Recovery. F. A. Roper, Brit. M. J. **2**:103 (July 15) 1933.

A case of encephalitis following vaccination, in a girl, aged 17, is reported. The patient recovered. Royster, University, Va.

The Decline in the Death Rate of Diphtheria Compared with That of Scarlet Fever. L. Cobbett, Brit. M. J. **2**:139 (July 22) 1933.

The author compares for England and Wales the remarkable decline in the death rate due to scarlet fever from 1891 to 1931 and the very slow decline in the death rate due to diphtheria in spite of specific therapy during the same years. Royster, University, Va.

Experimental Transmission of Poliomyelitis by the Digestive Route. C. Levaditi, C. Kling and G. Horms, Compt. rend. Soc. de biol. **112**:43 (Jan. 13) 1933.

By logical experimentation, the investigators have been able to show that a species of monkeys, Macacus cyanomolgus, is susceptible to the injection of poliomyelitis organisms into the digestive tract. This is not true for Macacus rhesus, the latter species, however, being very susceptible to intracranial inoculation.

At short intervals, animals of each species were given poliomyelitis emulsion (in potato) by mouth; in the rhesus type no symptoms developed, while the cyanomolgus monkey in about ten days presented paraplegia on the left side, and very quickly quadriplegia followed. At postmortem examination, the histologic changes typical of poliomyelitis were present, together with acute mesenteric adenitis.

It is therefore possible that Heine-Medin's disease can be induced in the monkey experimentally through the digestive tract. Wahl, Cleveland.

ANTIDIPHTHERITIC PROPHYLAXIS WITH SPECIAL MENTION OF VACCINATION. C. COMBA, Riv. di clin. pediat. **31**:769 (June) 1933.

This article presents a lecture in which is discussed the question of the prevention of diphtheria. Comba favors prophylactic injections of Ramon's anatoxin.

HIGGINS, Boston.

ENCEPHALITIS FOLLOWING PERTUSSIS IN AN INFANT. ALBERTO GAMBIRASSI, Arch. argent. de pediat. **4**:213 (March) 1933.

Encephalitis occurred in an infant, aged 1½ years, following an attack of pertussis of moderate severity. Persistent convulsions ushered in the attack. These were followed by choreiform movements and convergent strabismus. There was persistent clouding of the sensorium, and the patient showed a tendency to stupor and sleep.

Complete recovery occurred after persistence of the symptoms for several months. The physical development of the infant proceeded normally.

SCHLUTZ, Chicago.

PROPHYLAXIS OF DIPHTHERIA. ROIG RAVENTOS, Bol. Soc. cubana de pediat. **4**:293 (Aug.) 1932.

Ineffectiveness in the prophylaxis of diphtheria is chargeable to several factors, among them uncertainty as to the diagnosis, timidity in the use of an adequate dose of serum and want of necessary isolation and of antidiphtheritic vaccination. There is often unnecessary use of serum for children who could be watched.

The author suggests the mobilization of nurses for the wholesale collection of exudates from suspected persons, particularly in the poorer districts of the community.

In cases in which the diagnosis is doubtful, serum should be used early, freely and for a sufficiently long period. Schick tests are not necessary if children are generally immunized, especially when exposed to contagion. Injections of preventive serum should only be given to children in whom the infection is possibly incubating or who cannot be watched daily or to young infants in whom immunization is not practicable.

The author recommends extensive propaganda for both laymen and the members of the medical profession. Children with diphtheria who cannot be satisfactorily isolated at home should be hospitalized.

He recommends the establishment of individual hospital units for patients with diphtheria with a properly immunized nursing staff. He also recommends compulsory immunization.

SCHLUTZ, Chicago.

DIPHTHERIA IN BARCELONA. MARTINEZ VARGAS, Med. de los niños **34**:97 (April) 1933.

From 1915 to 1919 there were 127.4 deaths per year from diphtheria and croup; in the following five years, the death rate averaged 102.4 annually.

In 1927, there were 84 deaths from diphtheria in Barcelona, more than in any other year. The disease has been more common in boys, and the highest mortality occurred during the age period of from 1 to 4 years; the youngest child was 8 months and the oldest 9 years. Of the 108 patients admitted to the hospital, 64 received intubation, and in 6 a tracheotomy was done. The mortality was 20.3 per cent. In certain years the disease appeared in a more malignant form. In 1929, of 27 patients, 19 had laryngeal diphtheria. The explanation for this is that the parents were compelled to come to the hospital because the children were suffocating. Autopsy was performed in all of the fatal cases, and bronchopneumonia and cardiac insufficiency were found responsible for death in the great majority of cases. In one case that came to necropsy, that of a girl, aged 5 years, it was

found that, although there were no signs of laryngeal obstruction, the trachea and the bronchi were filled with the membrane. Diphtheria continues to appear in epidemics in Barcelona. Some cases seem to be resistant to serum, and occasionally malignant diphtheria is encountered, with such alarming symptoms as cardiac arrhythmia and dilatation, enlargement of the liver, cyanosis, vomiting and albuminuria.

DWYER, Kansas City, Mo.

THE PSEUDOREACTIONS OF SCHICK AND DICK. E. JAZO and T. H. HARGUINDEY, Monatschr. f. Kinderh. **58**:229, 1933.

The authors present a study of simultaneous Schick and Dick tests. They conclude that the pseudoreactions are due not to any common factor such as allergy or constitution, but to the specificity of the individual toxin.

GERSTLEY, Chicago.

TOXIC DIPHTHERIA: FURTHER OBSERVATIONS ON THE EFFECT OF PASSAGE OF DIPHTHERIA BACILLI THROUGH DIFFERENT NUTRIENT MEDIUMS ON TOXICITY. E. SIMON, Ztschr. f. Kinderh. **54**:487, 1933.

The passage of various strains of diphtheria bacilli through artificial nutrient mediums influenced the toxicity in both directions; i. e., some strains became more toxic, while others lost their toxicity.

SHELLING, Baltimore.

NEGATIVE PHASE AFTER IMMUNIZATION WITH DIPHTHERIA ANTITOXIN. A. HOTTINGER and E. QUACK, Ztschr. f. Kinderh. **54**:495, 1933.

In the course of immunization of nine children against diphtheria, repeated study of the antitoxin content of their serum showed that in six the antitoxin in the serum was labile. In one patient the antitoxin in the serum fluctuated widely; when it fell below 0.01 unit per cubic centimeter of serum (negative phase), diphtheria developed.

SHELLING, Baltimore.

## Chronic Infections

THE ROENTGEN SIGNS OF TUBERCULOSIS OF THE VERTEBRAL BODY. HOWARD P. DOUB and CARL E. BADGLEY, Am. J. Roentgenol. **27**:827 (June) 1932.

Correlation of the pathologic changes of tuberculosis of the spine with the roentgen findings is important. One hundred cases were studied; the average age incidence was 29 years. The average duration of symptoms at the first examination was six and one-half years. The hematogenous route of the infection is favored, but the lymphogenous route may also play a part. A suggestion is made that in some cases the primary infection may be in the disk. Roentgenologically, tuberculosis of the bodies of the vertebrae is divided into (1) the central type, (2) the intervertebral articular type and (3) the anterior type. Tabulation reveals that the central type is more common in the dorsal area and the intervertebral type is more common in the lumbar area. The central type causes collapse of the body of the vertebra in a high percentage of cases, while in the intervertebral type, the vertebral form (body) is preserved until late in the course of the disease. Narrowing of the disk is the earliest and most constant roentgen sign in tuberculosis of the spine. Abscess, the most common complication, was found in 84 per cent of the cases in this series at some stage of the disease. Skipped infection, or two areas of infection with normal vertebrae between, was found in 10 per cent of the cases. Concomitant tuberculosis was found in other parts of the body in fifty-three instances. The pulmonary lesion was the most common concomitant lesion and was found in twenty-four cases.

STULIK, Chicago.

VITAMINE THERAPY IN PULMONARY TUBERCULOSIS: THE EFFECT OF VIOSTEROL ON THE ABSORPTION, RETENTION AND EXCRETION OF CALCIUM. PAUL D. CRIMM, J. W. STRAYER, H. L. WATSON and G. HEIMANN, Am. Rev. Tuberc. **28**:202 (Aug.) 1933.

This experiment was carried out on two people, one a normal control and one with quiescent pulmonary tuberculosis, afebrile, and in the third stage. After a period of dietary stabilization, daily estimations were made of the absorption, retention and excretion of calcium before and after the administration of viosterol. Later, the action of the administration intravenously of physiologic solution of sodium chloride on the hypercalcemia was studied. From these experiments it appears that there is a direct correlation between the amount of intake of calcium and the output of fecal calcium. During the early administration of viosterol there is a decrease in urinary and fecal calcium. Continued administration increases the urinary calcium and decreases the fecal calcium. Viosterol increases the absorption of calcium, as indicated by the elevation of serum and urinary calcium. Increased dosage of vitamin D increases the absorption and the retention of calcium in the fluids of the tissues to effect a state of hypercalcemia. When physiologic solution of sodium chloride is administered intravenously, it is a specific antagonistic to a state of hypercalcemia effected by vitamin D.

EUGENE SMITH, Ogen, Utah.

TUBERCULOUS PNEUMOTHORAX IN INFANCY. JOSEPH GREENGARD and IRVING R. ABRAMS, Am. Rev. Tuberc. **28**:236 (Aug.) 1933.

Greengard and Abrams report two cases of tuberculous pneumothorax occurring in infancy. Such a pathologic condition is rare in this age group, since rapidly progressive tuberculous lesions in the lung in the nature of a primary infection tend to be complicated by marked early generalization by the blood stream and termination with the syndrome of generalized miliary tuberculosis. The symptomatology manifested by the two infants differed from that commonly observed in adults, in whom an abrupt onset with evidence of acute circulatory embarrassment and collapse are the rule. In these cases the onset was insidious, and the presence of air in the pleural space was found on routine physical and roentgen examinations. From a prognostic point of view tuberculous pneumothorax in infancy is to be looked on as a manifestation of a malignant type of infection. This is in direct contrast to the more common instances of nontuberculous pneumothorax, many of which are benign.

EUGENE SMITH, Ogden, Utah.

A STUDY OF CHILDHOOD TUBERCULOSIS IN DETROIT: A PRELIMINARY REPORT. J. A. JOHNSTON and HENRY D. CHADWICK, Am. Rev. Tuberc. **28**:244 (Aug.) 1933.

The children who formed the basis of this study were routinely examined on their admission to an agency for foster-homes. They were all white; practically all were American-born of foreign parentage, more than 50 per cent being Polish. Their economic status was low. The incidence of reaction to 0.1 mg. of tuberculin administered intracutaneously in this group of 2,500 children in Detroit from birth to 15 years of age was 14.3 per cent; in children in the age group from 5 to 15 years, it was 17.9 per cent. The incidence of a positive cutaneous test and roentgenogram was 4.4 per cent. During the first four years of the study two cases of the adult type have developed among 359 reactors, and the condition in both of the patients had been diagnosed previously the childhood type of tuberculosis.

EUGENE SMITH, Ogen, Utah.

TUBERCULOSIS IN CHILDREN. JOHN H. KORNS, Am. Rev. Tuberc. **28**:251 (Aug.) 1933.

More tuberculous infection and disease were found by examining the persons coming in contact with patients with diagnosed cases than by routine examination of apparently healthy school children. Tuberculin testing of large numbers of

elementary rural school children consumes time and is expensive. The infrequency of tuberculosis in this group of children would hardly warrant the routine use of this method. Tuberculin testing of high-school students is desirable in the hope that, by roentgen examination of the reactors, adult lesions may be discovered before illness causes the student to seek medical advice. Roentgen examination of the lungs should not be withheld when the tuberculin test is not allowed.

EUGENE SMITH, Ogden, Utah.

TUBERCULOSIS IN INFANTS AND PRIMITIVE RACES. WATHENA MYERS JOHNSON and J. ARTHUR MYERS, Am. Rev. Tuberc. **28**:381 (Sept.) 1933.

The first infection type of tuberculosis in infants, whether or not the lesion can be located, is rarely, if ever, fatal; but it results in allergy which makes reinfection from exogenous or endogenous sources dangerous. The first infection and reinfection types of tuberculosis are almost like two distinct disease entities as far as their attack on the body is concerned. In infancy and in all other age periods the type which usually results in disability and death is the reinfection or adult type. The use of tuberculin tests and x-ray films demonstrates the fact that the lesions in the chest of Indians and of white persons are identical. The higher incidence of positive reactors among Indians results from lack of preventive measures in the care of patients with open cases of tuberculosis among them. All positive reactors to tuberculin have the first infection type of tuberculosis and, therefore, have potential cases of the reinfection type of the disease. Therefore, since the incidence of positive reactors is so high among children, a high incidence of a destructive type of disease is to be expected among adults. Observations of Negroes show that they also react in the same manner to the first infection type of tuberculosis as do other races. The reaction to the first infection type among persons of Mexican nationality is apparently no different from that found in other races and nationalities. One of the most encouraging facts brought to light through recent observations and studies is that infants and primitive races have remarkable ability to control the first infection type of tuberculosis, and that apparently the only serious factor with which one has to contend in the control of tuberculosis among them is the communicability of the disease, as is true in all other age periods and in other races and nationalities.

EUGENE SMITH, Ogden, Utah.

THE PRIMARY, SECONDARY AND TERTIARY TUBERCULOUS STATES AND THE VALUE OF GASTRIC LAVAGE AS AN AID TO DIAGNOSIS. W. R. F. COLLIS, Irish J. M. Sc. Feb. 1933, p. 49.

Gastric lavage, with injection of the material into guinea-pigs, is of definite value. The Armand-Delille method is also of value, being more rapid, but not as often positive. Collis regards all children with erythema nodosum, phlyctenular conjunctivitis, pleurisy and benign infiltrations of the lung as having an open lesion. He stresses the importance of early recognition and treatment in a preventorium.

SNELLING, Toronto, Canada.

FREQUENCY AND SIGNIFICANCE OF TUBERCULOSIS OF THE TONSILS. THERESE RÖSSNER, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **135**:214 (July 14) 1933.

Rössner states that tuberculosis of the tonsils is probably always a secondary infection, originating by the hematogenous or lymphogenous route or in the sputum. The hematogenous route is the most probable in the opinion of the majority of authors. Tonsillar tuberculosis usually assumes a light form, and in the majority of cases it can be recognized only microscopically. Complications following the removal of tuberculous tonsils were rarely seen; in only a few cases was the operation followed by miliary tuberculosis. In the author's clinic, tuberculosis was found in 3 of 296 tonsils examined histologically, or 1.01 per cent. The statistics in the medical literature vary between 5 and 1.6 per cent.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

DOUBLE-SIDED PNEUMOTHORAX IN THE TREATMENT OF OPEN TUBERCULOSIS OF CHILDHOOD. MARGARETE RIED, Monatschr. f. Kinderh. **59**:24, 1933.

The use of double-sided pneumothorax for open tuberculosis is relatively new. Traditionally, it is held incompatible with life. Ascoli (1912) was the first to use the treatment.

In a study of 190 cases—in which girls were involved twice as frequently as boys—the writer found the treatment of inducing double-sided pneumothorax far more satisfactory than the older and more conservative treatment. Mortality under the old treatment was 75 per cent, against 6 per cent with the new. Ried again divides her cases into those discharged open and those discharged closed. It is not clear whether she means by this something connected with the technic, or refers to the discharge of tubercle bacilli in the sputum. At any rate, the mortality in each group was entirely in the open cases. GERSTLEY, Chicago.

ROENTGEN DIAGNOSIS OF ISOLATED TUBERCULOUS LYMPH NODES OF THE MESENTERY. E. A. VOSS, Monatschr. f. Kinderh. **59**:45, 1933.

Voss presents plates showing the possibility of diagnosing calcified tuberculous mesenteric lymph nodes by means of roentgenograms. GERSTLEY, Chicago.

ACTIVE IMMUNIZATION IN NEUROSYPHILIS WITH AVIRULENT STRAINS OF SPIROCHETES. L. BENEDEK, Monatschr. f. Psychiat. u. Neurol. **79**:33 (May) 1931.

In this preliminary communication Benedek reports the results obtained in treatment for neurosyphilis with cultures of living spirochetes made by Hilgermann. The organisms were rendered avirulent by a method not yet available for publication. A suspension of these organisms was injected intragluteally in doses of from 0.5 to 1 cc. every two weeks. On improvement, the dose was reduced to 0.1 or 0.2 cc. to avoid a too rapid binding of antibody, which would leave the organism defenseless. Four patients with tabes, three with the tabetic form of dementia paralytica and five with dementia paralytica were treated. The patients with tabes and those with the tabetic form of dementia paralytica showed marked improvement; visceral crises and pains disappeared, and in two cases the mental condition was favorably influenced. Good results were not obtained in the cases of dementia paralytica. The author believes that inoculations with Hilgermann's avirulent cultures undoubtedly have a beneficial effect on the neurologic processes observed in neurosyphilis. Further investigations of this method of treatment are being carried out.

ROTHSCHILD, Foxborough, Mass. [ARCH. NEUROL. & PSYCHIAT.]

THE DIETETIC TREATMENT OF TUBERCULOSIS OF THE BONE WITH THE DIET OF GERSON, SAUERBRUCH AND HERMANNSDORFER. J. ZELINKA, Časop. lék. česk. **71**:357 (March 18); 391 (March 25) 1932.

The author discusses the history and the development of diets up to the scheme of Gerson, Sauerbruch and Hermannsdorfer and includes the mineralogy of diet. The contemporary literature is reviewed. The Gerson, Sauerbruch and Hermannsdorfer diet is salt-free and spice-free, high in protein (90 Gm.) and fat (from 160 to 200 Gm.), low in carbohydrate (from 200 to 240 Gm.) and high in vitamins and minerals in the form of vegetables. The diet contains sodium antagonists like potassium, calcium, magnesium and bromine, and in some cases additional minerals of this type are added. The diets are outlined in detail as to quality, quantity and time schedule, and the cases of five of the thirty patients treated are cited in detail. The effect of mineralization was found to be efficient in tuberculosis of the bone with open abscesses, mixed infections and sepsis. Treatment over periods of from three to five months was gratifying even in hopeless cases and in those in which previous treatment was of little avail. Bibliography is included. STULIK, Chicago.

## Internal Diseases

INTESTINAL OCCLUSION BY ASCARIS. P. ANGHEL and DAVID, Bull. Soc. de pédiat. de Iasi **3**:128 (Dec. 19) 1932.

A child aged 3 years entered the hospital with acute intestinal obstruction. At operation a mass of round worms was found obstructing the bowel just above the ileocecal valve. The mass was broken up by manual manipulation and the parasites milked down into the cecum, relieving the obstruction, Santonin administered postoperatively caused the evacuation of three hundred and seven ascares.

LEMASTER, Evanston, Ill.

ENDOCARDITIS WITH LEUKEMIC REACTION. CAZAC AVERBUCH, Bull. Soc. de pédiat. de Iasi **3**:136 (Dec. 19) 1932.

One month after an attack of scarlet fever a boy aged 9 years become ill with fever, tachycardia and vague pains in the legs. An enlarged spleen was found. The differential blood count showed 2 per cent neutrophils, 95 per cent lymphocytes, 1 per cent mononuclears and 2 per cent plasma cells. After two injections of arsphenamine his general condition improved, the percentage of lymphocytes decreased, but a systolic heart murmur became apparent. After the third injection of arsphenamine a severe reaction, with generalized cutaneous rash and blood in the urine, occurred. The patient recovered from the acute illness, but a mitral stenosis indicating endocarditis developed.

LEMASTER, Evanston, Ill.

CONCENTRATION OF GUANIDINE-BASE IN BLOOD AND CEREBROSPINAL FLUID UNDER DIVERSE PATHOLOGIC CONDITIONS. E. PEKELIS, Gaz. d. hôp. **106**: 1417 (Oct. 4) 1933.

The normal value of guanidine in the blood is about 0.07 mg. per hundred cubic centimeters; over 0.2 or 0.3 mg. per hundred cubic centimeters is certainly pathologic. Epilepsy, Parkinson's syndrome, hypertension, poliomyelitis and multiple sclerosis were the diseases included in the study.

In only one of the twenty-four cases was the value below 0.5 mg. per hundred cubic centimeters. The highest values were found in epilepsy, and in this condition the guanidine concentration of the cerebrospinal fluid may definitely exceed that of the blood.

No constant relationship was found between creatinemia and guanidinemia.

KAJDI, Baltimore.

TWO CASES OF CHRONIC POLYARTHRITIS IN CHILDREN. MAFALDA PAVIA, Riv. di clin. pediat. **30**:1440 (Nov.) 1932.

Case reports are given of two children with arthritis. One patient, a boy of 5 years, had a typical case of Still's disease, with polyarthritis, fever and glandular enlargement; following a typical attack of measles, there was a remission of symptoms lasting two and one-half months. The other patient, a girl of 7 years, had symmetrical idiopathic polyarthritis; she was afebrile, and she obtained no benefit from any type of therapy, although drugs, glandular products and physical therapy were tried.

HIGGINS, Boston.

NONCAUSTIC INTERMITTENT ESOPHAGEAL OBSTRUCTION BEGINNING AT TWO AND ONE-HALF YEARS OF AGE. EMILIO ROVIRALTA, But. Soc. catalana de pediat. **2**:5 (Jan.-March) 1929.

The author believes that the etiology in the case reported was probably syphilitic mediastinal adenitis, a secondary spasmodic element accounting for the

intermittent nature. The initial response to antisyphilitic treatment lasted about a year. Contractures prevented a good permanent result.

WATSON, Elmhurst, Ill.

TREATMENT OF SEVERE CASES OF KALA-AZAR. M. TORELLÓ CENDRA, But. Soc. catalana de pediat. **3**:58 (April-June) 1930.

The criteria for judging severe cases of kala-azar are as follows: hyperacute form, increasing anemia, poor tolerance to antimony, chronicity and the presence of a complicating pathologic condition. If the infant is very anemic, a transfusion is advised before specific treatment is started. Emphasis is placed on making the treatment mild at first. In severe cases the author uses a pentavalent antimony prepared for intramuscular injection. Increasing doses and stronger preparations are used later. Many proprietary preparations are evaluated. Splenectomy is advised, provided the liver is not affected, when patients with chronic cases no longer respond to antimony. The persistence of enlargement and fibrosis of the spleen after successful treatment is another indication for splenectomy.

WATSON, Elmhurst, Ill.

KETOGENIC-ANTIKETOGENIC RELATION IN THE TREATMENT OF INFANTILE DIABETES. FELIX PUCHULU, Semana méd. **2**:1260, 1932.

A diet with a high ketogenic-antiketogenic quotient does not disturb development in children. Constant ketosis is dangerous even in the absence of glycosuria. For that reason, a diet with a quotient lower than 1 is recommended.

KUGELMASS, New York.

SARCOMA OF THE PLEURA NOT PREVIOUSLY DESCRIBED IN CHILDHOOD. ULLRICH NEUMANN, Arch. f. Kinderh. **98**:139 (Jan. 24) 1933.

Sarcoma of the pleura in a 3 year old child was diagnosed by the histologic appearance of the material obtained by aspiration of the chest. The diagnosis was confirmed at autopsy.

LEMASTER, Evanston, Ill.

THE DISEASE PICTURE OF AGRANULOCYTOSIS. ADOLF HARTWICH, Ergebn. d. inn. Med. u. Kinderh. **41**:202, 1931.

On the basis of ten cases personally observed, the author discusses the onset and course of agranulocytosis and the clinical symptoms, the etiology, the pathogenesis, the pathologic anatomy and the therapy of the disease. The author claims that the picture of sepsis that occurs in the disease is secondary to the necrotic processes in the skin and mucous membranes, for the cultures of the blood became positive only a few days before death, whereas at the beginning of the disease they were consistently negative. Local infections are undoubtedly chiefly responsible for the spread of the disease, and then toxic injury to the bone marrow follows. In one of the cases, arsphenamine seemed to play an etiologic rôle; in two cases, an endocrine disorder, and in two, disturbances of the liver. Agranulocytosis may be considered as a clinical entity with a variable etiology. The pathogenesis of the disease rests on a primary selective injury of the bone marrow, although occasionally there may also be an erythropoietic disturbance, and cases of agranulocytosis have been reported in which there was even simultaneous stimulation of the bone marrow. Roentgen therapy gave no therapeutic success, whereas, according to the author's observations. decided changes in the disease picture followed transfusions of blood: the transfusions influenced the temperature curve primarily; their influence on the blood picture was only transient. Finally, the author proposes to supplant the term "agranulocytosis" by "granulocytopenia" or "granulocythemia."

CAPPER, Philadelphia.

CLIMATIC, DIETETIC AND MEDICINAL TREATMENT OF ANEMIAS OF CHILDHOOD. CURT FALKENHEIM, Kinderärztl. Praxis **3**:193 (May) 1932.

Change of climate by a sojourn in the mountains or at the seashore is recommended for secondary anemia due to repeated infections. Large doses of inorganic iron are indicated in chlorotic anemia. The use of copper as an adjuvant to iron is in the experimental stage.

HUENEKENS, Minneapolis.

MENSTRUATION AND MENSTRUAL DISTURBANCES AT PUBERTY AND PREPUBERTY. HANS ALBRECHT, Kinderärztl. Praxis **3**:241 (June) 1932.

The author discusses the normal limits for the beginning of menstruation, as well as menstruatio praecox and menstruatio tarda. Recurring colicky abdominal pain in young girls before the first menstruation may be due to incarceration of blood in the vagina, uterus and fallopian tubes caused by atresia of the vagina. This atresia may be a congenital atresia of the hymen or due to inflammatory adhesions of the vagina, following measles, scarlet fever or diphtheria. The most important disturbance of menstruation is polymenorrhea, because it can sometimes be fatal. The causes and treatment are discussed, including medicinal and glandular therapy. The most frequent complication of menstruation is pain before and during menstruation, with systemic malaise. Anteflexion of a hypoplastic uterus may be at fault, but the author opposes surgical intervention except as a last resort. More often hyperirritability of the vegetative nervous system is responsible for the pain. Therapeutically, diet, hydrotherapy, gymnastics, modification of the tempo of living and even complete change of environment must all be considered in bringing about improvement. Menstrual difficulties are frequently worse after excessive physical exercise (athletics) or great mental strain (school examinations), and Albrecht questions whether the new mental and physical avenues open to women may not be the cause of the marked increase of dysmenorrhea.

HUENEKENS, Minneapolis.

HYPERINSULINISM. GEORG ROSENFELD, Monatschr. f. Kinderh. **57**:269, 1933.

A girl, aged 18, suffered for two years from weekly attacks of extreme weakness, shivering and profuse perspiration. The blood sugar content was low. The author made a diagnosis of hyperinsulinism and sought measures to control the condition. He found epinephrine and its analogs, racemic ephedrine and *p*-methylamino-ethanol-phenol tartrate, very satisfactory.

GERSTLEY, Chicago.

SPONTANEOUS PNEUMOTHORAX IN CHILDREN (from the Children's Clinic of the University of Warsaw). R. BORANSKI, Pediatria polska **12**:17, 1932.

The author reports thirteen cases of spontaneous pneumothorax in children from 1 to 12 years of age. He found four cases due to tuberculosis, three to pleurisy, two to empyema and three to pneumonia. Spontaneous pneumothorax requires individual attention. For treatment, the author used narcotics, oxygen, support of the heart, transfusions of blood and other remedies. There were seven deaths, and six patients recovered. Two of the four patients with tuberculosis died and two got well.

KRUPINSKI, Chicago.

BLOOD PRESSURE IN SCHOOL CHILDREN. R. BORANSKI and T. LEWENFISZOWA, Pediatria polska **12**:86, 1932.

More than one thousand children were examined, and their blood pressures recorded. The ages of the children varied from 7 to 15 years. The average systolic pressure was from 80 to 130 mm. of mercury; the average diastolic pressure, from 40 to 80 mm., and the average pulse pressure, from 30 to 65 mm.

The blood pressure rises in proportion to the age, weight and height. Except in girls 13 years of age, the blood pressure is higher in boys than in girls. The

blood pressure is higher in the fall than in the spring. Psychic factors often modify the pressure, so that it is advisable to take repeated blood pressures. Records of blood pressures serve as important clinical aids and should be used whenever possible.

KRUPINSKI, Chicago.

BLOOD DYSCRASIA RESEMBLING STILL-CHAUFFARD'S DISEASE. BAUMRITTER, BULABRADEK and CHODKOWSKI, Pediatria polska **12**:101, 1932.

The case reported was characterized by swollen joints, enlargement of the spleen and liver, glandular enlargement, extreme emaciation and a blood picture of 30 per cent hemoglobin, relative leukopenia and 70 per cent lymphocytosis. The author attempts to differentiate the condition from lymphosarcomatosis (Kundrat), myelosarcomatosis (Sternberg), chloroma, luekemia and lymphogranulomatosis. An attempt was made to treat the patient with salicylates and cinchophen, vaccine, the roentgen rays and ultraviolet radiation, all without success.

KRUPINSKI, Chicago.

QUANTITATIVE CATALASE DETERMINATION IN FECES AND ITS SIGNIFICANCE FOR THE DIAGNOSIS AND PROGNOSIS IN INTESTINAL DISEASES. S. KEMP and T. THUNE ANDERSON, Acta med. Scandinav. **78**:308, 1932.

The catalase content of homogeneized feces was determined in a specially constructed apparatus by using 10 cc. of hydrogen dioxide to 100 cc. of oxygen. The number of cubic centimeters of oxygen given off in three minutes is taken as a measure and is designated as the "catalase number." In normal persons this is usually less than 10 and does not exceed 17. In intestinal conditions such as chronic constipation, fermentative dyspepsia, chronic mucous colitis, chronic enterocolitis and achylia gastrica, the change in the catalase number of the feces is neither great nor frequent. In acute enterocolitis, dysenteries, chronic proctitis, intestinal cancer or tuberculosis the catalase number of the feces is frequently much increased. The fecal catalase activity may, of course, be obscured by the admixture of cellular vaginal discharge or by the admixture of blood, particularly through discharge from abscesses. The catalase content of the food has little if any effect on the fecal catalase, although an exclusive milk or egg diet causes an increase. Bile, on the contrary, seems to inhibit the catalase activity. Purgatives do not seem to have any special effect. Consistently low catalase numbers form a serious argument against the possibility of a severe intestinal disturbance but do not entirely exclude it.

KUGELMASS, New York.

CONTROL OF INFECTIONS OF THE UPPER RESPIRATORY TRACT. A. CZERNY, Acta pædiat. **13**:55 (June 6) 1932.

Czerny aims to strengthen resistance to infections generally by regulation of the diet and locally by the use of lactic acid to keep the infections from passing the barrier of the mucous membrane. Twice a day or oftener the child is given lemonade containing, in 100 Gm. of water, from 1 teaspoonful to 1 tablespoonful of 10 per cent lactic acid flavored with raspberry syrup. This regimen must be carried out for at least several months; a total of a few weeks is unavailing. The results are said to be brilliant.

No evidence for this claim is given.

MCINTOSH, New York.

FREQUENCY OF TRICHOCEPHALUS IN STOCKHOLM. TELEMAK FREDBÄRJ, Acta pædiat. **13**:83 (June 6) 1932.

In an examination of the stools of 325 children during the winter months, Fredbärj encountered 7 cases showing ova of Trichocephalus dispar (2.2 per cent). None of the stools gave a positive test for occult blood. Three of the infested children gave vague symptoms which could not be definitely ascribed to worms; 4 of them had a history of eating dirt.

MCINTOSH, New York.

GROWTH IN LENGTH OF INFANTS WITH PYLORIC STENOSIS. EINAR GAMSTEDT, Acta pædiat. **13**:94 (June 6) 1932.

The study is based on twenty-three cases of pyloric stenosis uncomplicated by other diseases. All of the patients were underfed, partly as a result of vomiting and partly in the course of nonoperative therapy. The conclusion is reached that underfeeding interferes with growth in length, though not to the same degree that it impedes gain in weight; in fact, growth in length may go on, though at a subnormal rate, even when the weight curve is falling. The most marked retardation of growth in length occurs in patients of low weight at birth and in those in whom undernutrition has commenced at an early age; in them the length of the body may be as much as 20 per cent below normal. The observations were not carried beyond the age of 5½ months.

McINTOSH, New York.

OSTEOGENESIS IMPERFECTA AND BLUE SCLERAE. C. GYLLENSWÄRD, Acta pædiat. **13**:111 (June 6) 1932.

The author describes the case of a patient more than 14 years of age who had deformed extremities at birth and who throughout her life suffered repeated fractures as the result of minor traumas, some occurring even during sleep. The patient had noticeably blue sclerae from birth on.

The literature dealing with this syndrome is complicated by lack of uniform terminology and by a variety of interpretations of the facts. The syndrome is comprised of three elements: blue sclerae, brittle bones and a tendency to early deafness. Although the anatomy of blue sclerae is only poorly understood, it is now generally agreed that this condition is a heritable character, behaving as a mendelian dominant. The tendency to brittle bones does not act like a mendelian character; it may or may not be associated with blue sclerae, and apparently sporadic cases may be encountered. The distinction once commonly drawn between osteogenesis imperfecta and osteopsathyrosis is artificial, being one of degree rather than of kind, and should be dropped; but it is permissible and useful to maintain a distinction between osteogenesis imperfecta congenital (which may be obvious at birth and often leads to death during the first few months of life) and osteogenesis imperfecta congenita tarda (in which the degree of fragility is less striking and fractures may not be brought about until the patient reaches an age at which he becomes subjected to more violent forces). Not only are all degrees of severity of this symptom possible, but in addition it is impossible to establish a correlation between the degree of severity and the frequency with which other cases occur in a particular family tree. The association of early deafness is perhaps merely fortuitous.

McINTOSH, New York.

THE USE OF THE KETOGENIC DIET IN THE TREATMENT OF URINARY INFECTIONS IN CHILDHOOD. H. F. HELMHOLZ, Acta pædiat. **13**:195 (June 6) 1932.

Controlled bacteriologic studies showed that the urine of patients who are in a state of ketosis has bactericidal effect when the $p_H$ is below 5.6; that even in the presence of marked ketosis, urine with a $p_H$ much more than 5.6 is unlikely to have bactericidal power, and that, in the absence of ketosis, a $p_H$ below 4.8 is necessary to produce bacteriostasis.

Brief instructions for the calculation and administration of a ketogenic diet are given. In some patients diet alone is not sufficient to render the urine acid to the desired degree; it must be supplemented by from 1 to 3 Gm. of ammonium chloride a day.

Infections of the urinary tract otherwise totally refractory have been cleared up within two weeks with these measures.

McINTOSH, New York.

DYSTROPHIA ADIPOSOGENITALIS ASSOCIATED WITH RETINITIS PIGMENTOSA AND POLYDACTYLISM. C. LOOFT, Acta pædiat. **13**:322 (June 6) 1932.

Three cases of the Laurence-Biedl syndrome are reported, two in one family. In all of these cases, as in many of those previously described, there was marked

mental retardation. The relationship of the adiposity to the Fröhlich syndrome and to pituitary dysfunction was discussed but was not elucidated by new data. The retinal changes were in all instances associated with hemeralopia. In one case the polydactylism lacked the classic triad. McIntosh, New York.

Diabetes Mellitus in Children. J. Tillgren, Acta pædiat. **13**:461 (June 6) 1932.

Diabetes is not such a serious menace to the child as it was in the preinsulin era. The successfully treated diabetic child grows and thrives normally, even though he must continue to take insulin all his life. McIntosh, New York.

Diagnosis of Lymphatic Leukemia in Childhood. Y. Åkerrén, Acta pædiat. **13**:501 (June 6) 1932.

The borderline separating lymphatic leukemia from lymphosarcoma is not sharply drawn, and many cases exhibit features common to both conditions. It is not uncommon for children to manifest an aplastic form of anemia in hematopoietic disturbances of various kinds, and in a certain number of cases more or less classic and invariably fatal lymphatic leukemia eventually develops. Two cases of this kind are described, both occurring in children 4 years of age. At first there was anemia with leukopenia and a relative increase in lymphocytes, the number of reticulocytes and platelets being diminished; enlargement of the lymph nodes, liver and spleen appeared relatively late. One case lasted less than two months; the other, seven months. In the latter instance autopsy showed the typical picture of lymphatic leukemia; infiltration of the bone marrow may have accounted for the sluggish regeneration of erythrocytes, granular leukocytes and platelets. The author warns against a premature diagnosis of aplastic anemia.

McIntosh, New York.

## Nervous Diseases

Equine Encephalomyelitis. Beatrice F. Howitt, J. Infect. Dis. **51**:493 (Nov.-Dec.) 1932.

The virus of equine encephalomyelitis may be recovered during the febrile period from cardiac and peripheral whole blood or blood serum of guinea-pigs, rabbits and horses. It may also be found in the liver, spleen and kidneys and in the suprarenal and salivary glands of the guinea-pig. Neutralization experiments in vivo and in vitro with antiserum were successful. Toomey, Cleveland.

Hemoglobinophilic Bacilli from Infantile Meningitis. Bernice E. Eddy, J. Infect. Dis. **52**:242 (March-April) 1933.

In nine cases of so-called fatal influenzal meningitis, gram-negative hemoglobinophilic bacilli were isolated. They grew only in the presence of blood in the medium; they produced indol, grew better when tryptophan was added to the medium, fermented dextrose, galactose, xylose and, in one instance, maltose and raffinose, and were pathogenic for young white rats. Toomey, Cleveland.

Familial Myoclonia Occurring in Three Successive Generations. F. G. Lindemulder, J. Nerv. & Ment. Dis. **77**:489 (May) 1933.

Myoclonia is characterized by sudden, short, regular or irregular lightning-like contractions mainly affecting the proximal muscles of the extremities and, rarely, those of the face. The intervals of these jerkings vary. The twitching is made worse by excitement and does not occur during sleep. This report deals with the case of a youth, aged 17, in whom myoclonia began at the age of 12 years. The

patient had no symptoms referable to the nervous system or other symptoms. He was a skilful ball player and a better player than average in billiards. He had a normal gait and no impairment of the voice. The family history was irrelevant, except that the father, the father's sister and great-aunt and the patient's sister suffered from the same condition. The great-aunt died at the age of 80. Parathormone and calcium gluconate given intravenously had no effect on the condition. Subjective improvement was obtained by the administration of scopolamine hydrobromide in doses of 1/150 grain (0.0004 Gm.) three times a day. Electrical treatment of various kinds had no effect.

JAHR, Omaha.

PNEUMOCOCCIC MENINGITIS COMBINED WITH STREPTOCOCCUS AND DIPLOCOCCUS CATARRHALIS. S. H. ASHMUN, Ohio State M. J. **29**:243 (April) 1933.

The author believes that early bacteriologic differential diagnosis of the various types of organisms that cause meningitis is essential. The prompt use of ethylhydrocupreine hydrochloride, given intraspinally when indicated, combined with the intravenous use of neutral acriflavine, and drainage of both the spine and the cisterna are necessary in certain types of meningitis. The author cites five cases to support this view. Two patients in whom pneumococci and streptococci were demonstrated died in spite of treatment, which was begun late. One patient recovered without specific treatment, and two in whom pneumococci, streptococci and Micrococcus catarrhalis were demonstrated by repeated culture recovered following treatment. The author uses 1 cc. of 1:1,000 solution of ethylhydrocupreine hydrochloride in sterile physiologic solution of sodium chloride to each 2 Kg. of body weight, divided into from four to six injections; one or more injections are given intraspinally until the spinal fluid is clear. He also uses from 20 to 30 cc. of neutral acriflavine solution given intravenously.

SANFORD, Chicago.

THE FAMILY PHYSICIAN'S RÔLE IN THE PREVENTION OF MENTAL DISORDER AND DEFECT. H. R. C. RUTHERFORD, Brit. M. J. **2**:188 (July 29) 1933.

This article is a general discussion along the line indicated in the title.

ROYSTER, University, Va.

CALCUTTA BRANCH: A CLINICAL STUDY OF EPIDEMIC CEREBROSPINAL FEVER IN CALCUTTA. U. P. BASU, Brit. M. J. **2**:291 (Aug. 12) 1933.

The author presents the report of an outbreak of cerebrospinal fever in Calcutta which was divided into two separate outbreaks by a relatively long period of intermission. The outbreak is studied epidemiologically, pathologically and bacteriologically. The diagnosis is discussed from the standpoint of symptomatology, as are the prognosis and the treatment.

ROYSTER, University, Va.

AN UNUSUAL CASE OF MENINGITIS ASSOCIATED WITH HAEMATURIA. L. MARGARET MASTERMAN, Brit. M. J. **2**:834 (Nov. 5) 1932.

A case of meningitis associated with hematuria is reported, and the author's commentary is appended.

The points of interest are:

1. The onset: The child was acutely ill, and the case resembled acute hemorrhagic nephritis—probably a manifestation of meningococcic septicemia.

2. The prolonged course and the late manifestations of meningeal symptoms: Nine days after admission, the child appeared to have cerebral irritation lasting from twenty-four to thirty-six hours; thirty days after admission, he showed rigidity of the neck and an extensor plantar response.

3. The rapid improvement after encephalography: This was probably due to the breaking down of adhesions or to the releasing of an encysted area, after which the chronic inflammatory process, shown by the increase in the number of cells and in the protein of the cerebrospinal fluid, ceased.

The points in favor of calling the condition a meningococcic infection are:

1. The herpes at the onset occurs in a considerable number of cases (Rolleston, J. D.: Acute Infectious Fevers, Brooklyn, Physicians and Surgeons Book Company, 1925).

2. There are large numbers of polymorphs in the cerebrospinal fluid, and in subacute cases meningococci may be very scarce.

3. Cases of meningococcic infection with an onset resembling nephritis have been described.

4. A prolonged course with relapses is one recognized form of meningococcic septicemia.

ROYSTER, University, Va.

TREATMENT OF CHOREA BY BATHS. W. S. C. COPEMAN, Brit. M. J. **2**:1054 (Dec. 10) 1932.

Forty-four patients with chorea of long standing, referred mostly from general hospitals, were treated without drugs, by means of a somewhat prolonged immersion in baths at neutral temperatures and by general (light) massage. A small control series was treated in the orthodox manner. It was found that the same result was ultimately achieved in both groups. The group receiving baths improved more slowly, but the ultimate incidence of relapses proved lower than in the group treated in the orthodox manner. It is probable that a combination of the two methods would prove a more successful measure than would either method separately. This could easily be arranged in the hospital, as no special apparatus other than an ordinary air-ring or a canvas bath-top cover to fit the bath in the ward is necessary.

AUTHOR'S SUMMARY.

CONGENITAL DEFICIENCY OF CONSCIOUS AUDITORY PERCEPTION OF WORDS (WORD-DEAFNESS). E. P. WEBER, Proc. Roy. Soc. Med. **26**:510 (March) 1933.

This case was reported in a boy, aged 3 years. The only words the child could say were "Da-da" and "Ma-ma." He understood everything that was said to him, and could make himself understood. He could play games and dance like other children. He showed great interest and curiosity in things. He was well built, and his physical examination showed no abnormality. He was the only child (the result of the only pregnancy), as was his mother. His mother was in an accident in a motor car when she was in the third month of pregnancy.

WILLIAMSON, New Orleans.

CEREBELLAR TUMOR. HUGH THURSFIELD, Proc. Roy. Soc. Med. **26**:575 (March) 1933.

This case occurred in a girl, aged 7 years. The history and physical examination of the case are given in the report.

WILLIAMSON, New Orleans.

CRANIAL NERVE PALSIES. J. ST. C. ELKINGTON, Proc. Roy. Soc. Med. **27**:302 (Jan.) 1933.

The patient, a boy, aged 9 years, had suffered from clubfoot on the right side and some wasting of the right leg. The upper part of the face was immobile, and the lower part was markedly weak on both sides. There was complete absence of outward movement of the eyes, but all other movements of the eyes and all other functions of the cranial nerves were normal. The tongue was wasted more on the right side than the left. A roentgenogram of the skull showed nothing abnormal. Lumbar puncture had not been performed. The condition was thought to be either a nuclear degeneration or a slowly progressive pontile tumor.

WILLIAMSON, New Orleans.

THE PONTILE-BULBAR FORMS OF ACUTE POLIOMYELITIS IN THE ADULT. G. ÉTIENNE, Ann. de méd. **33**:1, 1933.

Étienne describes a case of acute poliomyelitis which clinically presented a picture of ascending Landry's paralysis. It responded favorably to a combined intraspinal, intramuscular and subcutaneous injection of 100 cc. each of anti-poliomyelitis serum (horse serum of Pettit) and of macacus serum.

WEIL, Chicago. [ARCH. NEUROL. & PSYCHIAT.]

ACUTE NONSUPPURATIVE ENCEPHALITIDES IN CHILDHOOD. J. DAGNELIE, R. DUBOIS, P. FONTEYNE, R.-A. LEY, M. MEUNIER and L. VAN BOGAERT, J. de neurol. et de psychiat. **32**:550 (Sept.) 1932.

The authors describe a group of encephalitides associated with certain contagious diseases and eruptive fevers which have become notable in recent years. They believe that epidemic encephalitis has become much more rare since 1921; yet manifestations of acute encephalitis occur more and more frequently and are of poorly defined origin. One of the most common of these is postvaccinal encephalitis. The encephalitides following or associated with vaccination and infectious diseases are spoken of as parainfectious encephalitides. The authors describe a number of syndromes associated with these encephalitides: the convulsive syndrome, in which the convulsions may be generalized or focal, and are usually associated with fever, loss of consciousness and respiratory disturbances; a somnolent-ophthalmoplegic encephalitis characterized by somnolence, ocular paralysis and fever; a somnolent paretic syndrome characterized by somnolence and paresis of certain muscles, particularly of the muscles of the legs, and diminution or loss of tendon reflexes, and an irritative hyperkinetic syndrome, characterized by psychomotor agitation, fever and muscular contractions which simulate choreic movements. In the meningo-encephalitic syndrome, meningeal symptoms precede or coexist with encephalitic manifestations. Some infections described as serous meningitis may be of the meningo-encephalitic type. Finally, there is an encephalitic myelitic syndrome associated with bulbar and spinal changes as well as encephalitic manifestations. Parainfectious encephalitides have been recognized and reported but little understood, because of the paucity of histologic examination. Complications following vaccinia are most frequent, but they not infrequently follow other infections, such as scarlet fever, measles, influenza and bronchopneumonia. Although the actual number of cases is high, the percentage is low; the vaccinal type, for example, occurs in 1 of 2,400 vaccinations. The occurrence in one member of a family of several persons fails to justify the term epidemic. The complications may occur in mild as well as in virulent cases, the symptoms of encephalitis appearing after the patient has recovered from the infection. In postvaccinal cases, the somnolent paretic syndrome often occurs. In smallpox, myelitis is more frequent than ataxia; in varicella, ataxia and myelitis, in the order named; in measles, apoplectic forms; in whooping cough, the convulsive form, and in mumps, the meningeal form. The onset of nervous complications may be acute and severe, or the symptoms may become progressively worse.

Vaccinal encephalitis has a high mortality (from 30 to 40 per cent), but few sequelae (10 per cent); measles has a low mortality (from 10 to 15 per cent), but frequent sequelae (40 per cent); in varicella the mortality and sequelae are both slight. Determination of the prognosis is difficult because patients with cases which seem particularly severe and are associated with coma may recover, while those with cases which at first show mild symptoms may die. In children of less than 1 year, vaccinal encephalitis is about one tenth as frequent as in children of school age. Nervous complications may appear about twelve days after vaccination; for varicella, from four to six days after the eruption; for measles, from the third to the sixth day, and for German measles, on the third or fourth day. The authors consider the possibility of a specific neurotropic virus as the agent of all parainfectious encephalitides and of the primary acute disseminated encephalitis; however, such a virus has not been demonstrated. All present similar histopathologic

appearances, demyelinization and perivascular gliosis. The authors believe that the hypothesis of a specific neurotropic virus is not correct. They consider it possible that in smallpox, measles, German measles and chickenpox there may be an invasion of the nervous system by the organism of the disease. The toxic theory as put forth by Pedrau for vaccinal encephalitis has also been considered. The histologic lesions in the encephalitides of whooping cough appear somewhat different from those following the eruptive fevers. The possibility that these manifestations of encephalitis are the result of an allergic reaction is also considered.

The authors suggest the following classification of parainfectious encephalitides of children; (1) eruptive fevers with septicemic characteristics, vaccinia, measles, varicella and smallpox (scarlet fever and acute disseminated encephalitis might also be considered to belong to this group); (2) infections such as influenza, bronchopneumonia and neuritis; (3) whooping cough, and (4) the encephalitides following mumps. Mumps with neurologic manifestations is considered comparable to epidemic encephalitis and anterior poliomyelitis.

WAGGONER, Ann Arbor, Mich. [ARCH. NEUROL. & PSYCHIAT.]

RETARDATION OF SPEECH. SUZANNE BOREL, Presse méd. **41**:9 (Jan. 4) 1933.

It is necessary to distinguish between two types of backwardness in speech: the first, that due to an actual mental deficiency, and the second, that which is inconsiderately called backwardness but which is simply a delay in the use of words and which completely disappears within a year or more. Children with the first type respond to nothing in the way of teaching; those of the second type are very teachable and are of average intelligence or even brilliant. The development of speech may be divided into four stages: (1) that of isolated words, lasting generally from 12 to 18 months of age; (2) that of joined words, from 18 months to 2 or 2½ years; (3) that of independent phrases, from 2 or 2½ to 3½ years, and (4) that of the development of correct grammar and selection of words, approximately from 3½ to 5 years. Environment may influence the development of speech. Certain difficult phonetic combinations may be omitted or others substituted.

BIEKER, St. Petersburg, Fla.

ACUTE ENCEPHALITIS. JOSE MARIA MACERA and J. PEREYRA KÄFER, Arch. argent. de pediat. **4**:190 (March) 1933.

The condition occurred in a boy, aged 10 years; it began with simple phimosis. Meningo-encephalic symptoms, evidently due to some infectious process, suddenly developed. The initial meningeal symptoms were transitory but were followed by pronounced neurologic and psychiatric symptoms, such as shaking of the head, convergent squint and nystagmus, tonic and clonic convulsions, increased tendon reflexes, a positive Babinski sign, abolition of cutaneous abdominal reflexes, tendency to sleep, mental confusion and disorientation and, at times, confusional hypomaniacal states. Lumbar puncture sometimes aggravated the encephalitic conditions.

The patient recovered. SCHLUTZ, Chicago.

LESIONS OF THE CEREBELLUM IN MONGOLIAN IDIOCY, AND SOME CONSIDERATIONS ON THE PATHOLOGY OF THE CEREBELLUM. J. M. DE VILLAVERDE, Trav. du lab. d. recherches biol. de l'Univ. de Madrid **27**:111, 1931-1932.

This article is a description of the lesions demonstrated with the Cajal and Bielschowsky reduced silver methods in a case of mongolian idiocy. The lesions are not characteristic; a great number of Purkinje cells are missing, the remaining ones being generally arranged in groups of a few, separated by empty spaces. Often the cells show clear symptoms of degeneration. The baskets on the Purkinje cells generally are constituted by a small number of fibers, which are thicker than normal. Villaverde emphasizes that a basket has never been found without a cell in it, although on many occasions the fibers of the baskets are not

in contact with the cell bodies, and that the opposite may be true, i. e., that Purkinje cells exist without the corresponding basket. The climbing fibers often show degenerations. Villaverde rejects the theory that explains mongolian idiocy as a regression to an older phylogenetic type; he thinks rather of alterations in the endocrine metabolism which determine an incomplete development of the nervous system.

LORENTE DE NÓ, St. Louis. [ARCH. NEUROL. & PSYCHIAT.]

A CASE OF BILATERAL OCCLUSION OF THE POSTERIOR CEREBRAL ARTERY. F. G. VON STOCKERT, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **34**:23, 1932.

An infant, aged 15 months, was admitted to the clinic for nervous diseases in Halle with the following history: Birth and development were normal. At the age of 4 months the infant could sit up unsupported. At the age of 5 months convulsions appeared, which lasted all night, following which the infant was unable to sit up. Internal strabismus developed, with apparent inability to see objects in the left visual field. Examination on admission to the clinic revealed an unusually wide and flattened skull 46 cm. in circumference, 34 cm. wide and 33.5 cm. long. The child was unable to hold up its head or to sit or stand unsupported. Attention could be attracted by auditory but not by visual stimuli, although the pupils reacted somewhat to light. There was no motor weakness, but all spontaneous movements were purposeless. The muscle tone was normal. The patellar and ankle jerks were lively, and there was no clonus. There was a bilateral Babinski sign, with preservation of the abdominal reflexes. During the examination frequent lightning-like, generalized twitchings were observed. The fontanel was hardly palpable, and, except for a distended vein at the root of the nose, there were no evidences of venous stasis. Two days after admission, in order to relieve the hydrocephalus, a callosal puncture was undertaken under narcosis produced by chloroform. The calvarium was unusually thin, and the dura was under markedly increased tension. As soon as the cannula entered the corpus callosum about 12 cc. of cerebrospinal fluid spurted out through the cannula, and an equal amount spurted out around it. The brain, which had not been pulsating prior to the escape of the fluid, then began to pulsate. Following this procedure the temperature rose. The infant died twelve days later.

Necropsy revealed hypoplasia of the suprarenal glands and parenchymatous degeneration of the kidneys. The calvarium appeared asymmetrical and bulged over the left frontal and parietal lobes, which were covered with extensive hemorrhagic pachymeningitis of long standing. The latter produced pressure on the subjacent cerebral substance. There were no evidences of an inflammatory process. The sinus transversus as well as the sinus sigmoideus contained fresh thrombi; the longitudinal sinus was completely occluded by a yellowish-brown thrombus which was adherent to the wall of the vessel. The brain showed aplasia of the occipital and temporal lobes on both sides.

Histologic examination disclosed cystic, sclerotic changes in the parts of the brain supplied by the posterior cerebral artery, i. e., the occipital and temporal lobes, but not in the thalamus. The temporal lobes were considerably affected, except the two upper convolutions, including the deeper opercular convolution and a part of the third temporal convolution, which were relatively well preserved on the left side. The lesions were much more extensive on the right side, where portions of the first, second and third temporal convolutions were severely affected; the lobulus fusiformis, the lobus lingualis (gyrus occipitomedialis and lateralis) and the gyrus hippocampi had completely disappeared, whereas on the left side considerable portions of the cornu ammonis were intact. Some of the caudal portions of the gyrus fornicatus were destroyed. The mesial portions of the occipital lobe were also severely affected. The pathologic process extended cephalad and mesially almost up to the splenium, which was only partly affected. Accordingly, the lobus precentralis was least affected, but the precuneus was more involved, so that its posterior portion, as well as the cuneus, was partially

destroyed. As the lobus lingualis was also invaded, it may be said that the entire calcarine area within the lesion was affected. The lesions were of the nature usually observed in secondary degenerations following vascular occlusion.

KESCHNER, New York. [ARCH. NEUROL. & PSYCHIAT.]

PARALYSIS OF THE ISCHIATIC NERVE FOLLOWING INJECTIONS OF STRONTIUM QUININE CHLORIDE AND UREA. NEDELMANN, Deutsche med. Wchnschr. **59**:534 (April 7) 1933.

Budai and Hirsch recommended strontium quinine chloride and urea as a therapeutic agent against whooping cough. The preparation became popular in Germany, and it is claimed that it is much better than the whooping cough vaccine for the treatment of pertussis. It is similar in its pharmacologic effect to calcium; i. e., it decreases the irritability of the sensor and motor nerves. It is applied in the form of repeated intramuscular injections. Recently a few cases were reported which showed paralysis of the ischiatic nerve as an untoward sequel of the intragluteal injections. Although special care was taken in the Children's Hospital of Essen to inject the preparation into the upper outer quadrant of the gluteus region, paralysis of the ischiatic nerve developed in three cases, one on the eighth, another on the second and a third on the twenty-first day after the last intramuscular injection. Therefore, the author warns against the intramuscular use of the quinine-strontium urea preparation. Whether it is more effective when given by mouth than when given by rectum will be discovered in the future.

KERESZTURI, New York.

PATHOLOGY OF AMYOTROPHIC LATERAL SCLEROSIS. A. PEKELSKY, Jahrb. f. Psychiat. u. Neurol. **49**:74, 1933.

Four cases of amyotrophic lateral sclerosis, with a duration of ten months, four years, twenty-six years and three years, respectively, are reported. As the average maximum duration of amyotrophic lateral sclerosis is four years, the case of twenty-six years' duration is noteworthy. In this patient the first symptom was paresis of several months' duration, which was diagnosed as polyneuritis. Recovery from the polyneuritis was never complete; the patient had periodic attacks of pain in the limbs; the final stage developed in an apoplectiform fashion; the changes in the muscles observed at this time could not be attributed to the recent acute process, but must have been developing gradually. The short duration of the disease in the case that lasted ten months is attributed to the relatively early appearance of bulbar manifestations. The clinical course in all cases was that of a typical progressive motor disturbance, which began asymmetrically and gradually affected almost the entire musculature. In two of the cases the bulbar symptoms appeared after the spinal symptoms were advanced, and in another the bulbar and spinal symptoms appeared simultaneously. It seems, also, that in some cases bulbar symptoms may appear in an apoplectiform fashion. In two of the cases severe pains in the limbs were a feature throughout the disease. The cerebrospinal fluid was normal in every case. A correlation of the clinical picture with the histologic findings also confirmed the well established fact that marked structural changes occur in the central nervous system without clinical manifestations.

Relatively speaking, the histologic changes were similar in all cases. Whatever differences there were could be accounted for by the age of the patient and the duration of the disease. It is noteworthy that lesions were observed also in structures adjacent to the pyramidal and anterior horn cell systems, so that the disease apparently is not a pure systemic disease. The lesions were those not only of demyelinization, but also of axonal degeneration, which was observed in the form of scattered patches. There was no evidence of meningitis, meningopathy or radiculitis. The anterior horn cells seemed more affected in the caudal portions of the neuraxis. In the cervical region these elements were preponderantly atrophic

and sclerosed, whereas in the lumbar region they showed more lipoid and less sclerotic degeneration. Sclerotic as well as lipoid changes were also observed in the cells in various places in the gray matter of the cord and in the medulla. In some of the cases there were numerous small softenings and hemorrhages in the vicinity of the degenerated corticospinal tracts. Small foci of softening were observed also in the white matter of the anterior central convolution and in the pons. The author attributes the variations in the clinical picture to the presence of the miliary softenings in various regions near the pyramidal system.

KESCHNER, New York. [ARCH. NEUROL. & PSYCHIAT.]

TESTS FOR MOTOR DISTURBANCES OF THE SOFT PALATE. BÉLA FREYSTADTL, Klin. Wchnschr. **10**:406 (Feb. 28) 1931.

In complete peripheral paralysis the soft palate does not move voluntarily or involuntarily. Voluntary motion can be tested for by asking the patient to say "Ah" and watching to see whether the soft palate rises well or only slightly. In pyramidal paralysis, voluntary function is paralyzed as in phonation, whereas involuntary function continues. Involuntary motion may be tested by observing reflex swallowing movements. Touching the center of the posterior pharyngeal wall usually causes contraction of the muscles of the soft palate. When persons are insensitive to this test, the epiglottis may be touched, for with the adduction of the vocal cords there also sets in contraction of the velum. In lesions of the extrapyramidal tract, both voluntary and involuntary movements can be carried out but speech becomes nasal.

With paralysis of the soft palate it becomes practically impossible to puff out the cheeks. If a patient with marked nasal speech cannot puff out his cheeks, the lesion is either of the peripheral nerves or of the pyramidal tract. In these cases closing the nose will enable the patient to carry out this movement, but when the nose is released the air rushes out and the cheeks become flattened.

Puffing out of the cheeks tests also the functional integrity of the orbicularis oris muscle.

SILVERMAN, Syracuse, N. Y.

TREATMENT OF EPIDEMIC MENINGITIS BY INSUFFLATION. M. NUSKE, Monatschr. f. Kinderh. **58**:13 (May) 1933.

The writer developed the idea that failure in the treatment of epidemic meningitis might be due to insufficient drainage. Accordingly, he developed a technic much like that used in encephalography to blow residual secretion from the cerebrospinal system. Since 1924, he has had twelve cases. In five of these, the patients were treated with serum. Three recovered and two died. Seven were treated by drainage and insufflation. Four recovered and three died.

GERSTLEY, Chicago.

TREATMENT OF MONGOLISM. M. PFAUNDLER, München. med. Wchnschr. **80**: 351 (March 3) 1933.

In a short note on the treatment of mongolism Pfaundler states that roentgen therapy is not beneficial. Its use is based on the theory that mongolism is due to an endocrine dyscrasia, a theory which Pfaundler believes to be incorrect. In some cases administration of thyroid gland produces a nonspecific improvement; in others it may be harmful.

BRAHDY, Mount Vernon, N. Y.

ATYPICAL SYNDROME IN PITUITARY TUMORS. A. BINGEL, München. med. Wchnschr. **80**:1009 (June 30) 1933.

The diagnosis of pituitary tumor is readily made in patients with characteristic symptoms of acromegaly, dystrophia adiposogenitalis, diabetes insipidus and certain forms of cachexia. However, a tumor of the pituitary gland may be

present without the symptoms usually associated with it. Bingel reported several cases in which diagnoses such as neurosis, encephalitis lethargica, tabes dorsalis and multiple sclerosis were made by competent neurologists or internists. In one case, a routine encephalogram suggested a pituitary tumor, and in others the correct diagnosis was made at autopsy. Bingel advises that a roentgenogram of the sella turcica be taken in neurologic conditions which are at all atypical.

BRAHDY, Mount Vernon, N. Y.

CHOREA CAUSED BY THE TOXIC EFFECT OF NEOARSPHENAMINE. VICTOR OKTABEC, Česká dermat. **13**:232 (Dec.) 1932.

In a girl, aged 14, with hereditary syphilis toxic symptoms developed after she had received 1.15 Gm. of neoarsphenamine. She had high and irregular fever; severe exfoliative dermatitis developed; she experienced excruciating pain in the epigastrium, and severe chorea was present. The psychic and motor excitement increased in severity until a violent tossing of the body occurred which required ether anesthesia for control. Before the nervous symptoms subsided a series of multiple abscesses developed. The patient made a complete recovery. Judging from the pathologic changes in chorea, which include involvement of the central nervous system, particularly the basal ganglions, the author concludes that this unique case was caused by the toxic effect of neoarsphenamine on the corpus striatum, substantia nigra, thalamus and nucleus ruber.

SPINKA, Texarkana, Texas. [ARCH. DERMAT. & SYPH.]

THE MENTALLY DEFICIENT CHILD BEFORE COURT. J. PERL, Zycie dziecka **1**:124 (Oct.) 1932.

The author claims that all children who are mentally deficient should be treated differently than the normal child. Stern defined intelligence as a general ability to do things. Claparade discussed oligophrenia and classified persons so afflicted as: (1) idiots, who, according to Binet, have the mind of a 2 year old child; (2) imbeciles, who have a mind between that of a 3 and that of an 8 year old child, and (3) simpletons (*débils*) whose mind never develops above that of a 5 year old child.

All these types of children have to be institutionalized properly and treated differently than the normal child. In Poland the association known as the Friends of Children takes care of all these patients.

KRUPINSKI, Chicago.

CLINICAL AND PATHOLOGIC STUDY OF TUBERCULOSIS OF THE CENTRAL NERVOUS SYSTEM IN CHILDHOOD. V. P. JOUKOVSKY and V. N. ROUSSKIKH, Acta pædiat. (supp. 11) **14**:1, 1933.

Many of the facts and conditions described in this article are matters of common knowledge. The authors, working in Smolensk, are admittedly handicapped as regards library facilities. They call attention to the occurrence of disseminated tubercles in the choroid plexus and in the spinal meninges in some of their cases of tuberculous meningitis. Another patient with tuberculous meningitis and miliary tuberculosis showed extreme distention of the superficial vessels in the cerebral sulci and a large area of necrosis and hemorrhage in the left frontal lobe resulting from thrombosis; elsewhere throughout the substance of the cerebrum there were extensive hemorrhages. (It is not stated whether the venous sinuses were thrombosed.) Some effort is made to correlate the clinical signs with the pathologic changes found at autopsy, but the clinical data given are scarcely adequate to enable one to evaluate this part of the work. The authors discuss the relationship of tuberculous meningitis to antecedent infections and to bodily constitution. The frequent association of tuberculous meningitis with tuberculoma of the brain in childhood is cited.

MCINTOSH, New York.

VARIOUS TREATMENTS OF EPILEPSY, ESPECIALLY THAT OF THE KETOGENIC DIET AND ITS EFFECT ON THE ORGANISM. O. W. HAVREVOLD, Norsk mag. f. lægevidensk. **93**:1095, 1932.

The variations in the composition of the urine, blood and spinal fluid which result from the treatment of epileptic patients with a ketogenic diet (a diet rich in fat and poor in carbohydrates) and from the treatment with acid salts (in daily doses of from 0.5 to 1 Gm. of ammonium chloride and ammonium dihydrogen phosphate per kilogram of body weight were investigated. The results with a ketogenic diet were: Acidosis was apparent in the blood, urine and spinal fluid, and could be measured quantitatively. The content of acetone in the blood varied considerably, from 0.1 to 0.25 Gm. per thousand cubic centimeters, during a period of twenty-four hours, as the ketonic effect is greatest after meals. During the fasting state, no acetone is found in the blood. The spinal fluid has a higher content of acetone than the blood—from 0.15 to 0.5 Gm. per thousand cubic centimeters; small quantities are found also during the fasting state. Typical variations of the $p_H$ of the biologic fluids were observed: In the urine, the $p_H$ varies between 5 and 6.5; in the blood, the $p_H$ is practically constant—about 7.65; the alkali reserve of the blood is also practically constant. However, in the spinal fluid, in which the $p_H$ normally lies between 7.6 and 7.65, a ketogenic diet rapidly brings the $p_H$ down to about 7.5, the lowest value observed being 7.41. Results with acid-salt treatment were: The $p_H$ of the urine falls to about 5, and the $p_H$ of the spinal fluid to from 7.45 to 7.55. The reserve of alkali and the $p_H$ of the blood remain practically constant. The healing effects of the treatments, however, are rather doubtful. The methods used for the determination are described in detail.

KUGELMASS, New York.

## Diseases of the Ear, Nose and Throat

ALLERGY AS RELATED TO OTOLARYNGOLOGY AND PEDIATRICS. FRENCH K. HANSEL, J. Pediat. **3**:516 (Sept.) 1933.

In this review there is an analysis of the publications on allergy that has a relationship to both the otolaryngologist and the pediatrician. Special emphasis is placed on the differentiation of allergic and infectious nasal conditions. Consideration must be given to the factors which indicate an allergic basis, such as the family history, past history of allergic manifestations, presenting symptoms, tests of the skin and examination of the blood for eosinophils. From the otolaryngologic standpoint, the following procedures are of the greatest value—rhinoscopic examination, nasal smears, roentgenologic examination of the sinuses and histologic study of the nasal and sinus tissues. In allergic rhinitis the nasal mucosa is usually pale, whereas in infectious rhinitis it is injected. Eosinophils are numerous in the nasal discharge of allergic persons, whereas pus cells predominate in the discharge of persons with infectious rhinitis.

LEMASTER, Evanston, Ill.

THE TREATMENT OF ACUTE OTITIS MEDIA IN ACUTE FEBRILE CONDITIONS. T. O. GRAHAM, Brit. M. J. **2**:287 (Aug. 12) 1933.

In the early stage of acute otitis media abortive measures, such as rest in bed, administration of a purge, steam inhalations of tincture of benzoin, drops of warm glycerin and phenol solution and a rubber hot-water bag to the ear, may suffice to bring about resolution and cure. If this is ineffective, the drum membrane should be freely incised and adequate drainage of the tympanic cavity and of the mastoid antrum, via the aditus, afforded. This may bring about a restitution to normal of an infected mastoid. If fever persists in spite of adequate drainage and pain and tenderness in the mastoid increase, the patient is obviously not improving; mastoidotomy becomes imperative, and should not be unduly

delayed. By adopting such a definite course one may hope to avert the onset of the more serious complications of otitis media, namely, meningitis, lateral sinus thrombosis, cerebral and cerebellar abscess, facial paralysis, labyrinthitis and deafness, the treatment of which is outside the scope of this paper.

AUTHOR'S SUMMARY.

INTRABRONCHIAL ADMINISTRATION OF IODIZED POPPY SEED OIL (40 PER CENT) IN CHILDREN. P. CANTONNET, J. A. SOTO and HECTOR CANTONNET, Arch. de méd. d. enf. **36**:674 (Nov.) 1933.

The so-called Capurro method of bronchial instillation as developed in this clinician's practice in Uruguay is discussed by the authors in a contribution from the Institute of Pediatrics and Puericulture in Paris. Different technics have been utilized in the treatment of respiratory diseases by iodized poppy seed oil since the original work of Forestier and Sicard in 1922; that of Capurro, which is described in detail and satisfactorily illustrated, is preferred on account of its simplicity, economy of materials and freedom from untoward accident. AMESSE, Denver.

TREATMENT OF ACUTE NONDIPHTHERITIC ANGINAS WITH DIPHTHERIA ANTITOXIN. SAVAS NITTIS, Presse méd. **41**:1775 (Nov. 15) 1933.

Impressed by the remarkable improvement in cases of nondiphtheritic angina treated with diphtheria antitoxin, Nittis has treated a large series of cases in this way. He gives a detailed report of five cases, in which he used from 2,500 to 10,000 units of antitoxin, with almost immediate amelioration of symptoms. He cites Woodyatt's experience in United States army camps, giving antitoxin intravenously to all persons with angina without regard to laboratory reports. Under this routine the mortality from diphtheria dropped to zero, and the nondiphtheritic cases showed remarkable benefit. Reactions seemed to be traceable to certain brands of serum used. The excellent results obtained with the serum cannot be attributed to a reaction against foreign protein, as injections of milk were tried without results.

BIEKER, St. Petersburg, Fla.

ACUTE PURULENT FRONTAL SINUSITIS WITH OCULO-ORBITAL COMPLICATION: CEREBELLAR AND LABYRINTHINE PHENOMENA; OPENING OF BOTH FRONTAL SINUSES AND EXPLORATION OF THE RIGHT FRONTAL LOBE OF THE BRAIN; FIXATION ABSCESS; CURE. CANUYT, LACROIX and SCHEPENS, Rev. d'oto-neuro-opht. **10**:735 (Dec.) 1932.

A young girl, with an acute exacerbation of chronic frontal sinusitis on the right side but with no cerebellar or labyrinthine signs, was operated on, and external drainage was instituted. One week later heaviness of the head, vertigo and vomiting appeared, and the patient was unable to stand. Lumbar puncture relieved the symptoms temporarily and revealed a normal fluid, except that the pressure was slightly increased. Neurologic examination revealed prostration, a tendency to fall backward, an incorrect result in the heel-to-knee test, a bilateral Kernig sign, slight stiffness of the neck, vertigo, nystagmus to the left in all positions of the eyes, incontinence and difficulties of speech. Nineteen days after the original operation the left frontal sinus was opened, and the right frontal lobe was explored, with negative findings. A fixation abscess (aseptic abscess) was produced and opened five days later. Immediate improvement began, and recovery was rapid. There is no consensus as to the operative treatment in cases of acute suppuration of the frontal sinus with orbital complications. The authors believe that the sinus should be opened promptly and widely, with external drainage and without curetting the sinus walls or the nasofrontal duct. The curative action of fixation abscess in grave septic conditions is extolled.

DENNIS, Colorado Springs, Colo. [ARCH. NEUROL. & PSYCHIAT.]

ROENTGEN TREATMENT OF RECURRENT INFLAMMATION OF THE NASOPHARYNX. R. NIEMEYER, Monatschr. f. Kinderh. **58**:439 (Aug.) 1933.

In fifty-four children with severe recurrent infections of the tonsils and lymphatic tissue of the nasopharynx, roentgen treatments kept two thirds of them free from recurrence for two and a half years. In the remaining one third, infections which developed were much milder than previously. The general health of the children was also improved.

GERSTLEY, Chicago.

SURGICAL TREATMENT OF TONSILS IN CHILDHOOD. M. NADOLECZNY, München. med. Wchnschr. **80**:1124 (July 21) 1933.

This is a long article concerning many indications and contraindications for tonsillectomy. Simple enlargement of the tonsils requires tonsillectomy only when there are respiratory disturbances and changes in the voice. Suppurative infections of the tonsils are frequent in childhood and are usually harmless. These may occur between two and three times a year, but are not an indication for tonsillectomy. If the infection becomes chronic, the tonsils should be removed. Peritonsillar abscess is not always an indication for surgical intervention. Acute septic infections require immediate tonsillectomy. In chronic septic infections the value of tonsillectomy is questionable. In acute articular rheumatism preceded by angina, tonsillectomy is often beneficial, although recurrences may occur following pharyngitis. In muscular rheumatism, neuralgia and neuritis the effect is questionable. Acute glomerular nephritis, embolic focal nephritis (without nephrosclerosis), polyarthritic endocarditis, glandular fever and conditions found in carriers of diphtheria bacilli are frequently improved after tonsillectomy. In chorea, chronic nephritis, severe endocarditis and myocarditis the operation has no effect. Removal of the tonsils does not protect against diphtheria or Vincent's angina. Nadoleczny advises careful examination with rhinoscopy of all patients. He prefers tonsillectomy to tonsillotomy. An unnecessary operation is detrimental to the patient, the physician and the medical profession, because it destroys the confidence of the patient.

BRAHDY, Mount Vernon, N. Y.

THE PATHOGENESIS OF OTOGENOUS PARAPHARYNGEAL ABSCESSES. D. M. RUTENBURG, Ztschr. f. Hals-, Nasen- u. Ohrenh. **33**:25 (April 12) 1933.

One of the ways in which infection may be transmitted from the ear to the parapharyngeal space is via the lymph channels. Another way is by direct spread through the digastric fossa and along the digastric muscle to the retromaxillary fossa where the parotid gland is located. From there the infection may spread through the parapharyngeal space to the exterior of the tonsil. The other direct route is via the mastoid cells around the labyrinth or the floor of the tympanic cavity, which sometimes extend to the inferior petrosal sinus under the cochlea or along the carotid canal to the apex of the pyramid. Pneumatic cells in the anterior wall of the tympanic cavity may also develop toward the pyramid. The pus filling these cells may break through to the outside and pass along the eustachian tube to the parapharyngeal and retropharyngeal spaces. The spread of a carious process to the first cervical vertebra and from there to the parapharyngeal space is a fourth, rare form of pathogenesis. Rutenburg reports a case in which the infection followed the route of the mastoid cells and the eustachian tube, causing an abscess in the parapharyngeal space. From there the suppurative process spread beyond the parotid gland and the incisura santorini and broke out in the posterior inferior portion of the external auditory meatus. The same inflammatory process caused extradural trigeminal neuralgia and the syndrome of Gradenigo. The author calls attention to the fact that following the injection of a 10 per cent suspension of bismuth in oil into the fistula as a contrast medium the suppuration stopped, the temperature became normal, and recovery was rapid. An analogous instance of the favorable effect of injection of bismuth into a fistula was recently observed by him.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

TONSILLITIS WITH NEPHRITIS AND PERITONSILLAR ABSCESS DESPITE TONSILLECTOMY. V. HINSBERG, Ztschr. f. Hals-, Nasen- u. Ohrenh. **33**:77 (April 12) 1933.

Hinsberg reports one personal observation of an acute infection of the "tonsillar region" accompanied by nephritis several years after tonsillectomy and four cases of peritonsillar abscesses occurring despite tonsillectomy, two of which are personal observations while two are cases from the literature. These four cases show that despite tonsillectomy, and sometimes several years later, an abscess may be formed in the region of the scar which presents the typical picture of a peritonsillar abscess and which may heal spontaneously or after incision or may lead to severe sepsis and death. In one of the two cases from the literature a small part of the superior tonsillar pole remained after operation; in the other case also this probably occurred In one of the author's cases a piece of tonsillar tissue half the size of a pea was found in the scar; in the other case such a fragment appeared to have remained at the lower pole. These tonsillar remnants are probably to be considered as the focus for the abscess formation. How infection occurred is not certain. The practical interest of these observations lies in the fact that abscess formation may occur even after tonsillectomy and in the warning contained in them to avoid leaving even the smallest tonsillar remnants when performing tonsillectomy, especially on the upper pole.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

ROENTGENOGRAPHY OF THE TEMPORAL BONE AND ITS CLINICAL SIGNIFICANCE IN AURAL DISEASE IN EARLY CHILDHOOD. S. I. WULFSON, A. L. KAPLAN and E. I. IAROSLAWSKY, Ztschr. f. Hals-, Nasen- u. Ohrenh. **33**:88 (April 12) 1933.

Wulfson and his associates think that Sonnenkalb's method is best for roentgenography of the temporal bone in infants and small children. The head of the child is placed on the casette and loosely strapped, and the trunk is held in place by an assistant. An exposure of from one third to three fourths of a second is sufficient. The author has examined by this method 110 temporal bones (55 patients), including normal bones and bones with acute, subacute or chronic processes. In the examination of children up to 4 years of age, in normal cases the pneumatization periods of Wittmaack could be followed. A pathologic condition in any portion of the temporal bone becomes manifest in the roentgenogram. While on the healthy side the honeycombed structure of the antrum and periantral region is easily recognized, on the diseased side these areas are poorly differentiated or obscured. Zones of lesser density appear when the bone is attacked. When both sides are diseased and the roentgenographic images are similar, diagnosis may be less easy and careful comparison with the clinical data is important. The authors conclude that roentgenography of the temporal bone is valuable for the study of the development of the bone and for the recognition of pathologic processes exhibiting no definite clinical symptoms, and that serial examination in acute cases gives valuable diagnostic and prognostic aid.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

THE ROENTGEN PICTURE OF THE EPIPHARYNX OF CHILDREN UNDER NORMAL CONDITIONS AND WHEN ADENOID VEGETATIONS EXIST. KARL ERICH GROTH, Acta radiol. **14**:463 (Oct.) 1933.

In certain cases, diagnosis by palpation and rhinoscopy is difficult or unjustifiable. Roentgen examination skilfully done gives a clear picture of the size of the adenoid and of the space in the epipharynx and can be carried out, if necessary, during sleep. Lately Groth has examined patients with adenoids with the roentgen rays to discover to what extent the passage through the epipharynx is affected by different positions of the head and by sleep. The profile picture is best suited for the study of these relations. In a normal child in the upright position the

passage is seen to be broad and spacious and affected only inconsiderably by different positions of the head. With adenoid vegetations in the epipharynx the roentgen picture presents another appearance. A considerable swelling on the posterior pharyngeal wall represents the pharyngeal tonsils, and the soft palate appears as a shadowy band narrowing backward below the adenoid, with a thin lumen of air between, which indicates the narrowed epipharyngeal passage. The appearance is then practically the same whether the patient is in the recumbent or in the sitting position when the picture is taken. VINTON, Brooklyn.

## Diseases of the Skin

NEVUS PILOSUS PIGMENTOSA CONGENITA: ITS SKIN RESPONSES TO DRUGS. MORTON S. STERN, New England J. Med. **209**:694 (Oct. 5) 1933.

Hairy pigmented moles are congenital lesions. They vary from the size of a pinhead to a lesion which may cover nearly one-half the body. Two types of extensive nevi are relatively uncommon: the "bathing drawer" variety of pigmented and hairy nevi covering the region indicated by its name, and the more unusual, so-called 'tippet" nevi covering shoulders and upper part of the back. The pigmentation is mainly due to large quantities of melanin. Prenatal psychic emotions are commonly mentioned as an etiologic precipitating factor in most cases.

This study was undertaken to obtain information as to whether an abnormally pigmented and hairy area caused by increased ectodermal tissue differed basically in physiologic activity from the normal tissue. A case of pigmented and hairy nevus of the bathing drawer variety is presented in detail. The cutaneous reactions of the nevi and normal skin were compared and the following observations made: 1. The response of the abnormal skin to epinephrine was more rapid, more extensive and of longer duration. 2. The response of the nevus to atropine was more retarded, more extensive and of a longer duration than that of normal skin. 3. Histamine evoked a delayed reaction, a greater response and one of longer duration in the pigmented area. 4. The reaction to pilocarpine was delayed and of longer duration in the nevus than in the normal tissue. 5. Physostigmine showed practically no reaction in the nevus. GENGENBACH, Denver.

LICHEN URTICATUS OR URTICARIA PAPULOSA. GEORGE W. BRAY, Brit. J. Child. Dis. **30**:180 (July-Sept.) 1933.

From 10 to 20 per cent of all outpatients with cutaneous involvement at children's hospitals in England have papular urticaria. The wheal is evanescent and lasts from four to twelve hours, whereas the papule lasts several days or weeks. The latter appears on rather than in the skin. The intense itching leads to excoriation and the formation of a small crust; septic infection, however, rarely occurs to any degree. The lesions are practically confined to the covered parts of the body. Eighty per cent of the cases commence before the age of 3 years and the majority of the cases are found during the warmer months of the year.

From his study Bray concludes that two factors seem to be involved, one dietary, the other thermal. The dietary factor may be divided into two groups of foods: (1) the fats, especially bacon fat and other pig products, vegetable oils and fats, and cod liver oil; (2) such common foods as fish, egg, potato, oats and chocolate. The lesions cease to appear in the majority of cases when the fats mentioned are removed from the diet and care is taken not to let the child become overheated. LANGMANN, New York.

CLINICAL AND EPIDEMIOLOGIC SIGNIFICANCE OF ERYTHEMA NODOSUM IN CHILDREN. J. BROCK, München. med. Wchnschr. **80**:1087 (July 14) 1933.

Brock describes the clinical course of erythema nodosum. From data collected mainly in Scandinavian countries it has been found that in practically all children in whom erythema nodosum occurs it is a manifestation of tuberculous infection.

It frequently develops at the end of the biologic period of incubation, at the time when the skin first becomes sensitive to tuberculin. During the course of erythema nodosum the skin is highly sensitive to tuberculin, reacting to it in high dilutions. There is an increase in the rate of blood sedimentation. In many cases repeated roentgenologic examinations will show active lesions involving the pleura, parenchyma of the lungs or hilar nodes. Every case of erythema nodosum in childhood means a new tuberculous infection and indicates the presence of a carrier in the child's environment. This is of great epidemiologic significance. The treatment of erythema nodosum is that of tuberculosis.

BRAHDY, Mount Vernon, N. Y.

## Surgery and Orthopedics

WEAK, PRONATED AND FLAT FEET IN CHILDHOOD. HAROLD R. ROEHM, Arch. Pediat. **50**:380 (June) 1933.

Attention is called to the very large number of children showing defects of the feet in some degree, particularly weak, pronated and flat feet. The writer discusses the causes of flatfoot and describes a simple method of ready diagnosis. He describes in considerable detail the correction of flatfoot by the use of the Thomas heel. He further believes that the pediatrician is in the best position to prescribe and supervise the treatment of this condition.

WADDELL, JR., University, Va.

INFANTILE DEFORMITIES OF THE KNEE AND HIP. MAX BOHM, J. Bone & Joint Surg. **15**:574 (July) 1933.

This paper was presented at the meeting of the British Orthopaedic Association, London, in 1932, and is a review of the research work done by the author during recent years. His comparison of the anthropoid and the fetal, infantile and adult human development of bone in the hip and knee is interesting. If the development of the human skeleton above the stage found in the anthropoid ape is arrested, a deformity is produced, corresponding in kind to the stage of "arrest."

RYAN, Vancouver, Canada.

SURGICAL PEDIATRICS. HERBERT E. COE, J. Pediat. **3**:376 (Aug.) 1933.

The subject of this review is phrased designedly to emphasize the necessity of a pediatric attitude of mind on the part of any one who carries out surgical procedures on infants and children. The author summarizes and discusses briefly the most important recent contributions to the literature on conditions in children requiring surgical intervention. The following subjects are dealt with: the use of avertin as a basal anesthesia; routes for parenteral administration of fluids; the use of thorium dioxide; foreign bodies in the respiratory tract; the early correction of clubfoot; the treatment of burns with tannic acid; plastic surgery; appendicitis; intestinal obstruction; birth marks; splenectomy in purpura haemorrhagica, and urinary disturbances.

LEMASTER, Evanston, Ill.

TREATMENT OF SKULL AND BRAIN INJURIES. A. JOHNSON BUIST, J. South Carolina M. A. **29**:206 (Sept.) 1933.

Injuries are increasing, particularly to the skull and the brain. It is the damage which is done to the brain rather than that done to the skull that accounts for the seriousness of such injuries. "Our efforts should be directed first to the preservation of life and second to the restoration of the injured person as an economic asset to the community." In most cases there is a hypersecretion of cerebrospinal fluid, so that the normal mechanism of absorption is overtaxed, resulting in an increase in intracranial pressure.

Every case manifests shock, which is the primary condition to treat by rest, quiet, heat and proper drugs to prevent the loss of fluids. Omit the making of roentgenograms until this condition has been attended to.

Intracranial pressure is relieved best by repeated lumbar punctures. If there is a subdural hemorrhage or a rupture of a middle meningeal vessel, a subtemporal decompression is advised if conditions are favorable.

A sedative for restlessness is appropriate, but morphine is not advocated.

WESTON, JR., Columbia, S. C.

UROLOGY IN THE YOUNG. MAURICE MUSCHAT, M. J. & Rec. **138**:49 (July 19) 1933.

The pathologic pictures seen in the young, with a few exceptions, are identically the same as in the adult, only in miniature. The kidneys of the young have the ability to maintain their physical and biologic equilibrium in spite of tremendous obstacles. One encounters cases in which very little renal tissue is left and in which standard tests of renal function show practically the zero mark, yet the blood chemistry remains normal until the very end. In an adult, very little is necessary to change the renal equilibrium, to upset the normal balance of the blood level. Because of this ability of the kidney in the young, diagnosis of pathologic states is often not made. In many diseases of the kidneys, such as hydronephrosis (partially obstructed bladder), the urine is normal. Pyuria or hematuria appears later than one might expect. The urinary tract is often involved secondarily to another disease, such as tonsillitis or enteritis. Pyuria caused by the latter ailments clears up rapidly, but it does not do so if it is caused by partial obstruction. Primary pyuria in boys is very rare. It is usually caused by malformation or obstruction. Proper investigation of pyuria or hematuria should include history, physical examination, urinalysis, phenolsulphonphthalein test, blood chemistry, intravenous urography or retrograde cystography. The author then gives his technic for urography and cystography. He then mentions various pathologic conditions he has seen in children and suggests treatment for them.

WILLIAMSON, New Orleans.

CHANGES IN THE EPIPHYSIS SECONDARY TO INFECTION. JAMES WARREN SEVER, New England J. Med. **209**:62 (July 13) 1933.

Normal longitudinal growth of bone is dependent on a sufficient blood supply to the region of the epiphyseal cartilage plate. Reactions of the bone are many times the same to different mechanical, chemical and infectious stimuli, making roentgen interpretations of tuberculous, osteomyelitic and syphilitic epiphyseal changes, at times, very difficult. The changes in tuberculosis are largely destructive; in osteomyelitis, first destructive and then formative; in syphilis, largely formative. Characteristic roentgenograms are shown and discussed.

GENGENBACH, Denver.

CONGENITAL TORTICOLLIS: REVIEW OF THE PATHOLOGICAL ASPECTS. HENRY J. FITZSIMMONS, New England J. Med. **209**:66 (July 13) 1933.

Torticollis in early life usually is either congenital or traumatic-obstetric.

Of sixty-four children for whom the place occupied in the family was known, forty-three were the first children born to the mother. Of the remaining twenty-one who were not born of primiparae, sixteen were classified as born by "difficult prolonged labours," "cross-births" or "breech presentations." Of eighty-three births in which the history of the labor was known, only fourteen were described as normal, forty-six were "difficult" or prolonged, fifteen were "breech presentations," and eight were "cross-births."

The conclusions were that: 1. In all cases congenital torticollis results from fibrosis in the sternocleidomastoid muscle consequent on the development and

absorption of the so-called sternocleidomastoid tumor of infancy. 2. A sternocleidomastoid tumor, and therefore torticollis, results from a temporary acute venous constriction in the muscle, this obstruction taking place during labor. 3. It is probable that such a temporary venous obstruction has been rendered permanent by patchy intravascular clotting in the obstructed venous tree.

GENGENBACH, Denver.

ANAL FISTULA. E. PARKER HAYDEN, New England J. Med. **209**:376 (Aug. 24) 1933.

The author reports the results of a statistical study of 388 patients with anal fistula admitted to the Massachusetts General Hospital in the years from 1921 to 1930, inclusive, and gives interesting early historical references.

The ratio of males to females was 3 to 1.

There were only 3 patients under 10 years of age and 9 between 10 and 20 years; 90 per cent were between 20 and 60 years. Only 2.4 per cent of those examined pathologically were tuberculous.

The end-results in 280 cases show that 92 per cent were cured by complete incision and drainage.

GENGENBACH, Denver.

THE TREATMENT OF FRACTURES IN CHILDREN BY THE USE OF SKELETAL TRACTION. W. K. WEST, South. M. J. **26**:644 (July) 1933.

The major cases in which the use of skeletal traction is indicated are: (1) Cases of patients admitted to the hospital several days or weeks following the accident. (2) Cases in which there is serious involvement of the skin which interferes with the application of traction on the skin. (3) Cases in which there are multiple fractures, such as a fractured femur and a fractured tibia and fibula of the same leg. In this type, fixed skeletal traction is indicated; that is, the fractures are reduced and the fragments fixed by the introduction of wires, and they are held in the cast by the aid of metal bows. (4) Cases of malunion of the femur with sufficient shortening to warrant open reduction; this should be followed by wire-weight traction.

SCHLUTZ, Chicago.

PULMONARY ABSCESS IN CHILDREN. DAVID T. SMITH and ANGUS MCBRYDE, South. M. J. **26**:686 (Aug.) 1933.

The authors report six cases of pulmonary abscess in children, one due to bacteria, four to fusospirochetal organisms and one to Actinomyces. The differential diagnosis and the specific treatment are discussed.

SCHLUTZ, Chicago.

PHAGEDENIC ULCER OF THE NECK. D. P. R. KEIZER, Nourrisson **21**:178 (May) 1933.

A case of phagedenic ulcer of the neck, which is reported from Java, occurred in a boy aged 2 years. The main interest centers in the differential diagnosis. Other possibilities were cutaneous diphtheria, leishmaniosis, frambesia, mycosis, syphilis and tuberculosis. Cultures and smears from the base of the ulcer showed only fusiform bacilli and streptococci, proving the lesion to be due to infection with Vincent's bacillus. The sore healed promptly with the application of iodoform powder.

MCCLELLAND, Cleveland.

DIAPHRAGMATIC HERNIA. T. CENTENO, Rev. chilena de pediat. **3**:204 (May) 1932.

The author reports a case of diaphragmatic hernia in a child who had reached the age of 12 years. The herniation was on the left side of the diaphragm. The heart was displaced to the right to an extent that dextrocardia was simulated in

the roentgenogram. Variable resonance characteristic of gastric resonance was observed over the left lower part of the thorax, showing that the stomach had herniated into the cavity of the thorax. There were mild symptoms of cardiac insufficiency. The amazing finding in the case was the relative absence of any grave symptoms or disabilities up to the child's present age. The author makes no mention of the final disposition of the case.

SCHLUTZ, Chicago.

## Miscellaneous

STATISTICAL REPORT OF INFANT MORTALITY FOR 1932 IN 955 CITIES OF THE UNITED STATES, American Child Health Association, July 1933.

The infant mortality rate in the 943 cities of the birth registration area was 56.8 for 1932. This rate is computed from reports of 966,741 live births and 54,898 deaths among children under 1 year of age. This is the lowest rate attained since the compilation of these annual reports was begun in 1911 by the New York Milk Committee. The lowest previous rate was 61.2 in 1931. The present rate is thus 4.4 points lower than in any other year, and only half the rate twenty years ago. The almost uninterrupted downward course continues in the rate for the urban portion of the registration area since its formation in 1915. The infant mortality rate for each of the cities in this survey is recorded separately from 1916 to 1932 (this comprises the 943 cities in the birth registration area and 12 additional cities in the death registration area).

LEMASTER, Evanston, Ill.

THE DEVELOPMENTAL HEALTH EXAMINATION. T. WINGATE TODD, J. Pediat. **3**:415 (Sept.) 1933.

Whereas a medical health examination is an assessment of constitutional status, a developmental health examination is an assessment of specific progress in physical growth and maturation, in mental expansion, in emotional stability and in other aspects of normal healthy childhood. The conduct of a developmental health examination may be divided into five components: physical growth, physical maturation, orthodontic appraisement, psychologic assessment and sociologic appraisement. The significance of the physical measurements is discussed. Roentgenograms of the bones furnish an estimation of mineral reserves, a recognition of constitutional vulnerability and an assessment of physical maturation. The inclusive method of examination suggested by the author offers greater precision in defining the superior type of child and also the self-rectifying types of retardation.

LEMASTER, Evanston, Ill.

BODY FORM OF YOUNG PERSONS. WILFRIED ZELLER, Gesundhfürs. f. d. Kindesalt. **8**:79 (June) 1933.

The article is an attempt to apply the principles of constitutional anatomy as they have been developed by the German and French schools to the study of the body form of young persons. The author calls particular attention to the changes which are brought about in boys by the effects of bodily activity, particularly such as is called forth by daily labor.

REICHLE, Cleveland.

RELATIONS BETWEEN INTELLIGENCE, SOCIAL STATUS AND FECUNDITY. K. SALLER, Ztschr. f. Kinderforsch. **41**:369 (June) 1933.

This study was carried out in the rural districts of two sections in Germany, the population of which is distinctly more primitive than the average rural population. The study was suggested by the famous Jesuit biologist of Berlin, Dahlem Muckermann, who asserted that the healthy rural population could keep up the birth rate and populate the cities, which at present are suffering an actual loss

of population in Germany. He advised the state to support the rural population, since it seemed hopeless to restore a birth rate in academic circles which could keep the population even stable.

Saller examined the rural populations to discover whether the same law holds true for these districts as for urban districts; namely, that the birth rate increases as the intelligence and the social status decrease. He chose the two districts because they retained many of the old characteristics of preindustrial Germany and because one represents an almost purely Protestant and the other an almost purely Catholic population.

Saller discovered that the law holds true for the rural population of both districts. He makes no attempt to explain the differences in intelligence between the social classes, but expresses the opinion that they are due to inheritance and to environment. He believes that his work shows that Muckermann's proposal will not be fruitful of good results, as the source of increased birth rate in rural districts is families of lower native intelligence.

REICHLE, Cleveland.

FIRST, OR DECIDUOUS, DENTITION. CENEK SAITZ, Zubni lék. **32**:29 (Feb.) 1932.

The author reviews the history of dentition from the time of the ancient Chinese and gives citations from the literature from the time of Hippocrates. It is interesting to note that even in those early times there was knowledge of the prenatal influence on the primary dentition as well as an orderly description of the various ailments attributable to teeth even in the present day. The consensus is that teething is physiologic and that the diseases found during this period are not attributable to teething per se. It is surprising that the insignificant tooth should warrant such a mass of literature over a period of twenty-three centuries.

STULIK, Chicago.

"UNACTIVE CHILD." HELENA JAWIDZYKOWNA, Zycie dziecka **2**:1 (Jan.) 1933.

The author's observation of children with chronic tuberculous osteomyelitis in a sanatorium brought forth a constructive criticism of how to improve the treatment of these children and how to make them happy morally, spiritually and physically.

The strict confinement to the rules and regulations of the sanatorium, with the restriction of their activity, has created a very depressive effect on these children. The author suggests that besides a regular sanatorium program there should be classes in drawing, music, painting, manual training and foreign languages. This type of program would give the child opportunity to expand its energy and diminish eroticism, hysteria, melancholy and other conditions.

KRUPINSKI, Chicago.

BRINGING UP A CHILD. J. C. BABICKI, Zycie dziecka **2**:5 (Jan.) 1933.

Bringing up a child has two objectives: first, the development of all his inborn qualities, and, second, the furthering of his cultural life so that he may live as a good citizen. For the first, one should give a child the proper surroundings for physical and spiritual development, and for the second, one should bring him to the rhythm of general life, for to be free he must live according to the laws of society.

In order to bring up a child one must consider the parents, the surroundings or circumstances and the child itself.

The parents should be the regulators and organizers of the influences acting on his development. The circumstances or surroundings are the materials which the child absorbs or rejects and which help him to develop and acquire knowledge. The child is the central point at which all these forces of rearing accumulate. The parents or supervisors of the child must understand him. They must know that the child, like any other animal, has two most important instincts: (1) self-preservation and (2) specific or qualitative instincts. Self-preservation makes the

child an egotist, because he does only the things that he likes, while specific instincts have more of an altruistic quality, which usually is developed about puberty. From these instincts may develop later the following impulses: imitation, knowledge of creation, fighting, superiority and care. KRUPINSKI, Chicago.

SCHOOL FOR NEGLECTED CHILDREN IN KIETRZU POZNAN. ZOFIA DRWESKA DAERNIGOWA, Zycie dziecka **2**:12 (Jan.) 1933.

The child of today is the citizen of tomorrow. By bringing up children one determines the people of the country. The more schools, the less jails. Bringing up the child in fresh air is developing rapidly in Poland. Poland has many of these fresh air schools, but they are usually private, conducted by monks and nuns and accessible only to those who can afford to pay. Poland realized that there are many neglected poor children who could be brought up as good, healthy citizens. She determined to establish fresh air schools for the poor, despite the great economic depression. These schools cover 20 acres of land, 15 miles from Pozen, and can accommodate one hundred and fifty children.

The personnel of these schools is composed of two medical directors, one physician, two hygienists with a knowledge of pathology, one dentist, and two teachers. The equipment includes an isolation hospital, a first-aid dispensary, a drug room, a solarium and diathermy apparatus. The program for the children is scientifically arranged and is suited to each child. KRUPINSKI, Chicago.

LABOR PROBLEMS OF MINORS. JANNA MIEDZINSKA, Zycie dziecka **2**:33 (Feb.) 1933.

Labor problems of minors confront every civilized country. So long as the public does not acknowledge their importance and seriousness, the laws, rules and regulations instituted by governments will have little effect in solving the problem. In Poland, children 15 years of age are allowed to work in factories; however, the work must be light, and frequent vacation is given, so as not to interfere with their physical and mental development. Children are forbidden to work at night. When a child works in a factory, he is given medical examination before, during and after working to see what effect the work has on him. However, with all the precautions and laws, thousands of children in Poland are employed in small factories and other undertakings, because of the economic situation, and where government supervision is impossible. Normally, the child finishes preliminary school at the age of 14, and from that time until he is 18 he attends a continuation school which all children are compelled to attend. Thus the labor evil for minors is minimized.

KRUPINSKI, Chicago.

INFANT CARE AND INFANT MORTALITY IN DENMARK AND SCHLESWIG-HOLSTEIN. P. HANSSEN, Acta pædiat. **14**:369 (April 28) 1933.

In a rural area overlapping the Danish-German border and containing about 75,000 inhabitants, the infant mortality averages around 60 (deaths during the first year per thousand living births), and has in certain times been as low as 43—almost the limit to which this index can be reduced by the elimination of post-natal causes. The author ascribes this exceptional record largely to the high percentage of breast-fed infants. A willingness on the part of the mothers to nurse their infants is traditional in this population, and further encouraged by pamphlets distributed by the state, and by home visits made by community nurses trained in infant care, of whom there is 1 for every 1,400 inhabitants. It is noteworthy that the proportion of midwives in this area is particularly high, 1 for every 1,560 inhabitants.

MCINTOSH, New York.

FURTHER OBSERVATIONS ON THE INJURIOUS EFFECT OF LIGHT. C. W. HERLITZ, I. JUNDELL, F. WAHLGREN and H. BJERLÖV, Acta pædiat. **14**:606 (July 12) 1933.

Herlitz, Jundell and Wahlgren have shown that antirachitic substances (cod liver oil, ergosterol and egg yolk), when administered to animals in doses approximating those used therapeutically in man, may produce severe anatomic damage to the myocardium. Jundell and Bjerlöv have attempted to show that changes in the electrocardiograms of children may be produced by solar and ultraviolet irradiation in doses which far exceed those necessary to cure rickets but in no greater doses than those used for other therapeutic purposes. These experiments, however, eventuated in a negative sense. In order to amplify these experiments, the authors turned to animal experimentation.

Three groups of young (from 2 to 4 weeks old) mice were chosen. All were fed a standard ration consisting of unboiled whole milk, fresh white bread and steamed oats. Group I was irradiated daily with a Reenrink-Van Wijk lamp which emits light the wavelength of which falls between 280 and 300 millimicrons; the time of irradiation was one hour, and the distance between the lamp and the subject was 70 cm. Group II was irradiated similarly with a lamp emitting light of a wavelength of 250 millimicrons. The third group served as controls. A fourth group was placed on a standard rachitogenic diet (McCollum 3143). Electrocardiographic records were made of the animals in the first three groups at regular intervals. Most of the animals showed no changes at autopsy. Although the lamps were efficient in protecting against rickets, neither of the two experimental groups showed electrocardiographic or anatomic changes indicating injury from the irradiation. The authors draw the conclusion that the margin of safety between the therapeutic and the noxious dosages of radiant energy of the wavelengths used is wide.

McCUNE, New York.

# Society Transactions

## CHICAGO PEDIATRIC SOCIETY

*Clinical Meeting, Jan. 16, 1934*

M. L. Blatt, M.D., *in the Chair*

Atonic Rachitic Stomach. Dorothy H. Welker.

This 6 month old colored female infant was admitted to the Cook County Hospital in November 1933, with symptoms of vomiting and fever, which had been present for two weeks, and a protuberant abdomen. The child had been breast fed but had not received any antirachitic therapy.

The physical findings and the results of roentgen examination of the long bones were characteristic of moderately severe rickets. The serum calcium was 8.6 mg. per hundred cubic centimeters, and the inorganic phosphorus, 4.3 mg. A flat roentgenogram of the abdomen, taken a few days after admission, showed a greatly dilated stomach filled with gas. Four fluidrachms (14.8 cc.) of cod liver oil was given daily; the vomiting ceased within one month, and the clinical picture improved. The stomach, however, remained dilated throughout a two month period of observation.

It appears that the distention of the stomach and the accompanying vomiting were part of the picture of the generalized atony of smooth muscles occurring in rickets.

Tuberculosis. Dr. Henry E. Irish.

This patient was admitted about six weeks ago because of rhinitis, which was so severe that the upper lip was excoriated. The discharge was serous. Cultures for Klebs-Löffler bacilli and streptococci were negative. A survey was made to ascertain the possible syphilitic status of the child, but x-ray pictures of the bones were normal, and serologic examination of the parents and child gave negative results. In the course of a routine tuberculin test a marked reaction occurred. This test was repeated a few days ago and the reaction is still active, showing a vesicular response.

The nasal discharge persisted and remained constantly negative for any specific organism, but has gradually decreased and now has almost ceased.

Roentgenograms of the chest showed a large central shadow; coming up at the border of the heart was a mass which occupied the central portion of the mediastinum and which presented a winged appearance. A shadow also projected from the hilus, showing typical tuberculous infiltration and also epituberculosis. Repeated examination showed this shadow to be constant. Lateral views did not help much in making a diagnosis. The original interpretation of the shadow was that it represented the thymus gland. Later, fluoroscopic examination revealed a visible pulsation, which was thought to be synchronous with respiration by one observer and with the heart beat by another. It was thought that the mass was possibly an anomalous auricle or an anomalous lobe of the lung.

Comparing this case with another which was apparently identical, I have here a picture of the chest after three roentgen treatments had been given for enlarged thymus. The reduction in the size of the mass and the change in the winged appearance gave the impression that it was a large thymus gland. The pulsation in the case studied may have been transmitted by the heart beat or, possibly, by respiration.

The interesting feature was that a case of primary tuberculosis presenting rhinitis or, possibly, otorrhea brought up the question whether there may have

been a process in the nose resulting in prolonged effusion on an allergic basis. Similar findings have been encountered in the eye and in the thoracic cavity, with a few tubercles or none. Large effusions occur in the subarachnoid space in meningitis, with minute pathologic changes, and the question has arisen whether severe otorrhea of four weeks' duration could have been due to an allergic response in a child infected with tuberculosis.

A Case for Presentation. Dr. Craig Butler.

R. B. was born in April 1933. The mother was an octipara and had had one baby weighing more than 10 pounds (4,535 Gm.), the others having been about average size. This child weighed 13 pounds and 1½ ounces (5,939.3 Gm.) at birth. The mother's thirty-two hour labor was terminated by a low forceps delivery, the shoulders being delivered with considerable difficulty. The baby lived and was the largest born in the Cook County Hospital who survived longer than the new-born period.

Examination on the first day revealed brachial plexus palsy on the right and cyanosis of the face, with petechial hemorrhages. The abdomen was flaccid. On the third day the child stopped nursing, was in a condition of marked shock and became pale and dehydrated. Fluids were given in large quantities, and blood was given intramuscularly. The abdomen was found to be doughy and distended. A diagnosis of abdominal hemorrhage was made, and 100 cc. of blood was injected intravenously. The condition improved. A mass developed in the right lower quadrant, and a triangle of ecchymosis appeared above the umbilicus. This faded within a week, and the abdomen gradually softened. The child began taking food and left the hospital in good condition, having regained his weight at birth. He is now 9 months old and weighs about 24 pounds (10,886 Gm.). Under the care of the orthopedic department the arm has improved markedly.

Mediastinal Abscess. Dr. Joseph K. Calvin.

Harry Z., aged 4 years, was brought to the hospital on Jan. 9, 1933. He had had a sore throat three weeks previously, which had lasted one week. Then he complained of pain in both ears, and one week before entering the hospital the right drum was incised, with slight drainage. He still complained of pain in the left ear. Fever had been present to some extent for three weeks. A slight cough was present.

The past history of the patient and the family history were without significance.

Examination on admission to the hospital revealed a slender white child, febrile, but alert and lively. The temperature was 101 F., the pulse rate 94 and the respiration rate 24. The only other positive findings were purulent drainage from the right ear and a reddened, bulging left ear drum. This was incised, and a purulent discharge resulted. The leukocyte count was 22,000, with 80 per cent polymorphonuclears. The Mantoux test and the urinalysis gave negative results.

Because of the slight cough and fever persisting for the previous ten days, a roentgenogram of the chest was taken, even though repeated physical examinations of the chest had given negative results. To every one's surprise, this revealed a large, well circumscribed tumor mass occupying the superior mediastinum. This could be immediately differentiated from other midline mediastinal tumors by the lateral cervical view, which showed marked anterior displacement of the trachea and eosophagus. As there were no pathologic changes in the cervical or dorsal vertebrae, the shadow was thought to be a mediastinal abscess behind the esophagus, originating in the retropharyngeal space and burrowing down.

No stridor, severe cough or dyspnea was present, only an occasional cough. The results of examination of the pharynx, larynx and upper portion of the esophagus were reported negative by the department for diseases of the nose and throat.

After two weeks in the hospital, during which the boy was active and playful, though some fever persisted, the condition became definitely more septic, and the temperature ranged to 104 F. He was then seen by a surgeon, who advised

exploration of the tumor through the back. However, several days later the child coughed and spat up purulent material; another roentgenogram revealed air in the tumor, indicating rupture into the esophagus.

Bacteriologic smears of the pus revealed many gram-negative diplococci in chains.

Within the next few days a mass was noted in the left posterior pharyngeal wall at the level of the base of the epiglottis. This fluctuated and so was incised; it yielded a profuse amount of foul-smelling, thick, yellowish pus.

The fever and cough gradually subsided. Three months after admission the mediastinal mass had disappeared, the symptoms had subsided and the patient was discharged as well.

DISCUSSION

DR. M. L. BLATT: After we obtained the roentgenograms showing the mass in the chest on careful reexamination, it was impossible to demonstrate the mass by percussion. There were no changes in the breath sounds. Furthermore, the child showed none of the difficulties of respiration which one might expect, and, aside from slight aphonia, showed no evidence of serious illness.

CARDIOSPASM. DR. PHILIP ROSENBLUM.

This girl (a Negress) is 12 years old and is shown because children are often brought to the Cook County Hospital with symptoms of disturbance of the digestive tract, and it is often difficult to interpret the symptoms. It is hard to get a child to cooperate so that good roentgenograms can be taken and it is not easy to interpret the roentgenograms. This patient presents a condition not seen often in childhood although it is common in adult life.

The trouble started about one year ago. Tonsillectomy was performed about that time, and a few weeks later the patient complained of difficulty and pain in swallowing both liquids and solids. This increased until about four weeks before admission, which was one month ago. She then had considerably more pain, vomited and had difficulty in breathing. Roentgenographic examination showed a typical sausage-shaped dilatation of the esophagus. This condition is usually associated with more or less neurotic persons, the hyperesthetic type. The child stated that she was not particularly worried about the tonsillectomy, but that the symptoms developed soon afterward. There was a question whether the condition was due to cardiospasm. We have been unable to find any organic pathologic changes; the Wassermann reaction was negative, and we found nothing abnormal except secondary anemia. No pathologic condition was seen with the esophagoscope. Cardiospasm is often associated with pathologic changes in the left lobe of the liver. No one as yet has found a sphincter muscle at the cardia. The question is, What produces the spasm at the cardia? Nervous, thoracic and abdominal disorders must be considered.

The patient has been given atropine and phenobarbital, without benefit. The department for diseases of the nose and throat has attempted dilation through the esophagoscope, and some improvement has been noted. This will be continued before more radical surgical procedures are advised. The results of the latter are not always encouraging.

CONGENITAL CYST OF THE LUNGS (SOLITARY). DR. H. M. JACOBS.

This 4 month old child was admitted to the Cook County Hospital on Dec. 13, 1933, with a dry hacking cough and vomiting of four days' duration. There had been no previous symptoms. Delivery had been normal. This was an only child.

Examination showed a well nourished female Negro infant who appeared acutely ill. There was tympany over the entire right side of the chest, with absence of breath sounds. The heart seemed to be displaced to the left, and there were a few fine râles in the left side of the chest.

Roentgen examination showed apparently complete absence of the markings of the right lung with displacement of the heart to the left.

The diagnosis rested between pneumothorax and congenital cyst of the lung. A needle was inserted into the chest and attached to a water manometer, and the initial pressure was so great that most of the water was forced out of the manometer, after which it showed normal respiratory fluctuations. A second attempt brought the same result, and we concluded that some sort of valvular action was creating pressure within the chest. The child became progressively worse and died two and a half days after admission.

Necropsy showed marked displacement of the heart to the left. The upper lobe of the right lung was composed of a huge single cyst, and the middle and lower lobes were compressed and airless. When the cyst was opened, two small slits were seen in the upper half, through which the bronchus communicated with the cyst. A small flap came down over the bronchial openings and closed off the bronchus in a valvelike fashion. About eleven cases of large solitary congenital air cysts have been reported in the literature.

URINARY RETENTION. DR. CHARLES K. STULIK.

This boy is 8 years of age. Birth was normal. The early, developmental and familial histories reveal nothing of importance. He has had measles, chickenpox and whooping cough; all these were uncomplicated. He has been vaccinated and inoculated with toxin-antitoxin.

He has had enuresis practically since birth and has had frequent and painful urination since the first of this year, accompanied by some abdominal distress, anorexia and malaise. The enuresis has been complicated with periodic attacks of frequency and incontinence. In spite of these he felt well until two months ago, when, during a period of two weeks, his ankles and wrists were successively swollen and inflamed and he had a persistent fever. After apparent recovery frequency, burning and pain during and after urination began and was followed by pain low in the lumbar region on the right. Dribbling of urine was almost constant. The malaise and anorexia were associated with abdominal pain, and a severe chill occurred just before his admission to the hospital.

Examination revealed a subicteric pallor and fair nutrition and development. He had dental caries, and the pharynx was injected. Examination of the chest gave negative results, and the abdomen was soft, except for slight resistance about the bladder. The bladder was grossly palpable.

The Mantoux test gave a negative result. The urine showed a few white cells and a trace of albumin; the urea nitrogen was 16 mg. and the sugar 80 mg. A cystogram was normal. A roentgenogram of the chest showed an increase in the markings on the hilus of the right lung.

Rectal examination revealed a smooth, hard, nodular mass in the prostatic area, involving the neck of the bladder.

The differential diagnosis rested between a congenital bar (sclerotic dam), with inflammatory reaction following recent infection; paralytic bladder; sarcoma; tuberculosis; urethral diverticulum; spina bifida occulta; calculi; a posturethral valve with inflammatory reaction, and dyschesia (fecal ampullation of the rectum, with retention of urine).

The urologist thought that the mass might be a sarcoma of the prostate. However, roentgenotherapy resulted in rapid diminution in the size of the growth. This points to an inflammatory reaction following the infection of several months ago. I think that the underlying cause is most likely a congenital bar at the neck of the bladder, and that inflammation has enlarged the prostate so that it simulates sarcoma. We are waiting for further developments before making a definite diagnosis, but I wish to make a plea for careful rectal examination in this type of case.

Another child was brought to the Cook County Hospital with the same type of disorder, and physical examination gave negative results. Rectal examination showed a massive fecalith, with pressure on the base of the bladder and spilling over of urine.

Not infrequently we see children with diarrhea and on rectal examination find a fecalith causing paralysis of the lower part of the rectum and incontinence of stool.

The common reaction is the congenital bar in the trigon of the bladder, which at times leads to secondary inflammatory reaction, with formation of a sarcomatous mass. This child has done fairly well on belladonna and codeine.

FULMINATING RICKETS. DR. A. LEVINSON.

This 14 month old Negro girl was admitted to the Cook County Hospital because of a cough and fever of four days' duration. There was no history of contact with tuberculosis. The patient was born at full term. The first tooth erupted at the age of 7 months, but the child has not yet learned to walk.

On admission, the patient appeared acutely ill and rachitic, with beading and flaring of the ribs, a protuberant abdomen and a square head. Roentgenologically bronchopneumonia was demonstrable, as were pathologic fractures in both femora and both humeri, some destruction of bone, marked demineralization of the bones and some periostitis.

Chemical examination of the blood confirmed the diagnosis of rickets; the phosphorus was 1.9 mg. per hundred cubic centimeters, the calcium 9.2 mg. and the urea nitrogen 17.75 mg.

The patient was given viosterol in doses of 15 minims (0.9 Gm.) three times daily and calcium lactate in doses of 15 grains (0.9 Gm.) three times daily. Two days after the viosterol was first given the blood phosphorus was 2.6 mg. per hundred cubic centimeters, and the calcium was 9.4 mg. The dosage of viosterol was increased to 30 minims (1.8 Gm.) three times a day, with marked improvement in the condition of the bones. Five days after the treatment was begun, roentgen examination revealed definite evidence of healing of the bones.

SCURVY. DR. REUBEN I. KLEIN.

This girl is 14 months old. She was admitted to the Cook County Hospital on Nov. 26, 1933. She was supposed to have partial paralysis of the upper and lower extremities as a result of poliomyelitis which occurred five weeks previously.

Physical examination showed a pale and irritable child with slight beading of the ribs. The gums were purplish and bled easily on pressure, but there were no other signs of a hemorrhagic diathesis. Both lower extremities moved little on stimulation, and the patellar reflex was absent on the left. The right arm was held motionless, and a soft, tender swelling with crepitation was noted at the shoulder. A roentgenogram disclosed the classic signs of scurvy, with an epiphyseal separation at the right shoulder and at the lower end of the left femur. The child was given 15 ounces (443.5 cc.) of orange juice daily, and within three days the gums were healed. A tender swelling at the lower end of the left thigh was noted on the fifth day of treatment.

After eleven days of therapy the swellings had diminished in size, were much less tender and had become hard. All the deep reflexes were present and normal at this time. A roentgenogram taken on the twenty-eighth day of treatment showed a large calcifying subperiosteal hematoma of the right humerus and of the left thigh.

The history disclosed that the child had been artificially fed from the age of 6 weeks; she received an adequate milk formula, but had never taken orange juice well. She received less than 1 ounce (29.5 cc.) a day of the latter and many days received none. At the age of 11 months, six weeks before the onset of the pseudoparalysis, 3 ounces (88.7 cc.) of prune juice per day were given.

This case illustrates the confusion that sometimes arises between scurvy and poliomyelitis and the effect of substituting prune juice, which has practically no vitamin C, for orange juice. It demonstrates that subperiosteal hematomas are not seen on roentgen examination until after antiscorbutic therapy has been administered and calcification has begun.

OSTEOGENESIS IMPERFECTA CONGENITA. DR. JULIUS H. HESS.

This is one of two children of a physician. The child is almost 3 years of age, having been born in March 1931. At birth she did not move the extremities well, and examination revealed four fractures in the left lower extremity and a fracture of the left clavicle. She is of fair intelligence.

As may be noted in the roentgenograms, fractures are present in practically all the long bones of all the extremities. The patient also had a large thymus. She was given roentgenotherapy for the thymus during the first year of life, with marked diminution in the size of the thymus shadow following treatment. While the fontanels are still well open, this condition has improved.

She has had orthopedic care at intervals since the fourth month, but is so uncomfortable under traction that the orthopedist does not like to carry out any strenuous measures.

She has had almost everything in the way of treatment. When I first saw her she was getting 3 teaspoonfuls of cod liver oil daily and had had some viosterol. This was increased to 15 drops three times a day, and later she received 15 drops daily of a 1:10,000 (McCollum-Simonds standardization) strength preparation, which is equivalent to about 1,500 drops of ordinary viosterol. The results have not been striking. Other forms of therapy included use of ventriculin with iron for a year and a half, administration of large doses of calcium and dicalcium phosphate and ultraviolet irradiation, during periods when the viosterol was not given. However, there has been no particular improvement, except in mental development and in growth and calcification of bone in the upper extremities. The lower extremities responded much less satisfactorily.

At all times the blood calcium and blood phosphorus have been high.

OSTEOGENESIS IMPERFECTA CONGENITA. DR. H. M. JACOBS for DR. GATEWOOD.

This 14 year old boy was admitted to the surgical ward on January 4. He gave a history of feeling something snap while he was being pushed in a coaster wagon. He has had fifteen fractures involving the legs, hips and clavicles, and has had open reduction four times. There has been no similar condition in the family.

He has characteristic deep blue sclerae; the teeth are in fair condition. There is an old healed fracture of both clavicles, with marked deformity, pronounced pigeon breast and severe deformity of both forearms. There is a scar over the right hip at the site of an open reduction, and on admission he had recent deformity of the left hip, with complete eversion.

Although roentgen examination has not been entirely confirmatory to date, the clinical impression has been that this is a case of osteogenesis imperfecta. The boy now is in a double spica cast.

GLYCOSURIA IN CHILDREN. DR. R. SPAETH.

Within a period of a few weeks four children have been admitted to the Cook County Children's Hospital with forms of glycosuria ranging from relatively benign to malignant. These cases have afforded us the opportunity of studying the practical application of the principles involved in the renal threshold, the blood sugar levels during fasting, the dextrose tolerance test and the employment of dextrose intravenously in the treatment of diabetic coma.

The first case was that of a malnourished white boy, aged 6 years, who was admitted with what was considered an acute abdominal condition. The urine showed large amounts of sugar without diacetic acid. Following the usual preoperative treatment with insulin, about twenty-four hours after laparotomy in which no appendicitis was found the patient passed into a state characteristic of diabetic coma with ketosis. With heroic doses of insulin and intravenous injections of dextrose, checked by determinations of the blood sugar every three hours, the ketosis was relieved within six hours. Immediately after subsidence of the coma and within the past three weeks since discharge, the urine has been con-

sistently free from sugar, without administration of insulin, and the patient has been on a diet liberally high in carbohydrate and protein. This case is illustrative of transient glycosuria with a severe infection of the upper respiratory tract, with concomitant abdominal lymphadenitis, confirmed by laparotomy. The influence of ether anesthesia in causing ketosis must be considered in this case.

The second patient is a 15 month old boy, who was admitted in a precomatose state, with sugar (4 +) and diacetic acid in the urine. Under expectant treatment with relatively small doses of insulin and subcutaneous injections of dextrose, the patient passed into a state of diabetic coma about four hours after admission. Although dextrose was given in large quantities by gavage, with insulin in proportionate amounts, the establishment of a normal blood sugar of 100 mg. was not associated with the disappearance of diacetic acid from the urine. The clinical picture was alarming, the patient appearing to be near death. Under treatment with a continuous intravenous drip of 5 per cent dextrose for thirty-six hours, with insulin given empirically under the guidance determinations of the blood sugar every three hours, the patient was out of the coma eight hours after this vigorous treatment was instituted. A day later, symptoms of hypoglycemia, with severe convulsions, developed, and respiration and normal heart action were reestablished under epinephrine, caffeine and intravenous injections of dextrose. With meals every three hours followed by insulin, the patient's urine has been kept almost sugar-free, and he is making excellent progress. The necessity of using intravenous injections of dextrose (an apparent paradox) and large doses of insulin checked by frequent determinations of the blood sugar, the danger of hypoglycemia in very young patients and the possibility of bringing patients in severe diabetic coma to recovery are demonstrated in this interesting clinical picture.

The third case is that of a 4 year old boy who was recently admitted with a history of pains in the back and extremities, fretfulness and fever of twelve days' duration. It was stated that one sister had diabetes. Physical examination revealed multiple subcutaneous abscesses of fairly generalized distribution, emaciation and low-grade fever. Laboratory studies demonstrated staphylococcic septicemia, with corresponding organisms in the lesions; persistent marked glycosuria; normal blood sugar during fasting, and normal sugar tolerance curves on repeated occasions. Roentgenograms of the chest and long bones were normal. There were no reactions to tuberculin. Because of the persistent glycosuria, with normal blood sugar determinations, this case is being tentatively considered one of renal glycosuria. The influence of the infection is obscure, as renal inflammation has not been demonstrated by examination of the urine on repeated occasions.

We have found it feasible to make repeated and rapid determinations of the blood sugar in our emergency ward by employment of a simple test tube colorimeter. This outfit is obtainable from the Denver Fire Clay Products Company at Denver. The determination requires 0.1 cc. of blood taken from a finger, which is easily obtained by pricking the finger with a sharp surgical knife blade. The chemical procedure is that set up for the micro-method of Folin and Wu.

SEPSIS LENTA. DR. MAURICE SCHNEIDER.

A 13 year old girl with no previous illnesses was admitted to the hospital eighteen months ago with typical multiple arthritis and a systolic murmur, which disappeared within three weeks under treatment with salicylates. She returned within one week with recurrent multiple arthritis. The heart was now enlarged, and a systolic and a presystolic murmur were present. Electrocardiographic tracings showed partial heart block. Blood cultures showed no growth. Thrombosis of the popliteal vein developed. After two months she was discharged to a home for convalescent patients with heart disease, where she remained five months.

She returned a third time to the hospital with a diffuse petechial eruption; the temperature was 103 F. Roentgenographic examination showed a normal-sized heart; no murmurs were audible. Blood cultures showed no growth. Electro-

cardiographic tracings were normal. There has been a septic temperature for eight months; the heart is still normal in size, and no murmurs are present.

The laboratory findings show no cause for the persistence of the fever. The Wassermann reaction is positive. Repeated blood cultures, agglutination tests, roentgenograms and electrocardiograms show no abnormality. The cause of the sepsis is unknown.

MENINGOCOCCIC MENINGITIS. DR. MEYER A. PERLSTEIN.

It is well known that meningitis in infancy may assume bizzarre forms. In this case not only were the symptoms grotesque, but the complications and course were unusual.

A 16 month old white girl showed an infection of the upper respiratory tract and otitis media six days prior to admission to the Cook County Hospital. Physical examination on admission revealed an acutely ill child with slight pharyngitis and bulging of the right membrana tympani. The latter was opened. Nine days later, mastoiditis developed on the right, necessitating surgical intervention. At this time the first and only symptom of cerebral involvement became apparent in ankle clonus. There was no rigidity of the neck, no bulging fontanel and no Brudzinski's or Kernig's sign. Lumbar puncture revealed purulent fluid with 4,000 polymorphonuclear leukocytes. Because of the preceding otitic and mastoid infection and because a smear of the spinal fluid revealed gram-positive intracellular and extracellular cocci and diplococci, no antimeningococcic serum was given. The child was treated instead by forced spinal drainage and continuous intravenous administration of hypotonic solution. Moderate clinical improvement ensued; the spinal fluid became clear; the cell count dropped to 400 lymphocytes, and the organisms disappeared from the smear. Repeated cultures were sterile.

Because the fever persisted, however, exploration of the lateral sinus was made twenty-five days after the child's entrance to the hospital. Following this exploratory operation, which revealed no thrombosis of the lateral sinus, there was an exacerbation of the meningeal symptoms. The spinal fluid again became purulent; the cell count rose to 4,300, and cultures became positive for meningococci.

Treatment with antimeningococcic serum was instituted. The temperature dropped to normal again; the acute toxic symptoms disappeared, and the spinal fluid again became clear, the cell count dropping to 250. However, clinical improvement did not accompany the bacteriologic and laboratory signs of cure.

At this time, eleven weeks after entrance, the child presents the typical picture of chronic basilar meningitis with hydrocephalus. There are spastic paresis of the right upper extremity and enlargement of the head, which is kept retracted. In addition, the child is deaf and blind. Deafness is a common complication of meningococcic meningitis. It is usually complete and permanent and is due to involvement of the eighth nerve. In this instance the hearing, which was absent, is slowly returning, so that the patient can be waked by loud noises. Ophthalmic complications are also frequent in meningococcic meningitis, and when blindness occurs, it is usually secondary to uveal or ocular infection or to optic neuritis. In this patient, however, there are no abnormal ocular findings except the evident amaurosis.

The fundi are normal, and the pupillary reactions to light, both direct and consensual, are present. This fact would place the lesions posterior to the geniculate ganglion and most likely in the cortical zones for vision. Such cortical amaurosis is rare in meningococcic meningitis.

This case presents the following unusual features: (1) meningococcic meningitis following otitis media and mastoiditis, (2) meningitis in which the first and only symptom was ankle clonus, (3) improvement of the meningococcic meningitis for one month following forced spinal drainage without serum treatment, (4) exacerbation of the meningeal symptoms following exploration of the lateral

sinus, (5) development of chronic basilar meningitis associated with hydrocephalus, (6) apparent improvement of complicating internal ear deafness and (7) central blindness without any apparent lesion of the peripheral visual apparatus.

HEMOLYTIC STREPTOCOCCIC MENINGITIS, WITH RECOVERY. DR. S. J. NICHAMIN.

This condition has a terrifically high mortality. Streptococcus haemolyticus was isolated in only thirteen of the forty-nine cases recorded in the literature in which recovery took place. In the majority of these cases the source of the infection was otitis media. A great variety of procedures, many of them heroic and radical, have been used in the treatment of this disease. No rational therapy has as yet been developed. In this case, after an initial injection of antimeningococcic serum, a simple mastoidectomy was performed. The remainder of the therapy consisted of a blood transfusion and repeated drainage of the spinal fluid by lumbar puncture.

The patient is 9 years old. She was admitted to the hospital on Feb. 16, 1933. She had been well except for a discharge from the ear two years previously; this occurred two weeks before admission, with headache, sore throat and pain in the right ear. The patient was put to bed for about a week, and the symptoms subsided. Two days before admission fever, pain in the back of the head, dizziness and projectile vomiting developed. Weakness became marked. The child was delirious on the day she entered the hospital. During the aforementioned period of two weeks several members of the family had influenza.

The patient had the usual diseases of childhood. The family history is not significant. Three brothers and one sister are in good health.

Examination revealed a well nourished and well developed white girl lying on her side in moderate opisthotonos. The temperature was 105.8 F.; the pulse rate was 148, and the respiration rate 28. There was marked rigidity of the neck. Brudzinski's and Kernig's sign were positive. There were no petechiae in the skin or mucous membranes. The right aural canal was filled with a thick purulent discharge. There was no tenderness or swelling over the mastoid. A mucopurulent secretion was noted over the posterior pharyngeal wall. The heart and lungs were normal; the liver and spleen could not be palpated. There were no masses and no tenderness in the abdomen. The Babinski reflex could not be obtained; the abdominal reflexes were absent; the knee jerks were not elicited.

Examination of the urine gave negative results. The blood count showed 21,000 leukocytes, with 81 per cent polymorphonuclear leukocytes. Lumbar puncture was done, and 45 cc. of cloudy spinal fluid was obtained. The cells numbered 1,650, most of which were polymorphonuclears. The Pandy test gave a reaction of 2+. Antimeningococcic serum (15 cc.) was given intraspinally. No organisms were seen on smears. Culture of the spinal fluid showed a pure growth of gram-positive lancet-shaped diplococci, and a subculture showed a pure growth of hemolyzing streptococci.

Consultation with the department for diseases of the ear, nose and throat was obtained, and a simple mastoidectomy was performed soon after the patient's admission. The postoperative condition was fair. The rigidity of the neck was marked and remained so for several days. The temperature ranged between 104 and 106 F. Repeated spinal punctures were performed, one every other day, totaling four; following this the child showed definite improvement. Cultures of the spinal fluid obtained by these tappings showed no growth. A blood transfusion was given about six days after operation, and the child showed clear evidence of improvement. The temperature became normal; the patient appeared more alert, and there were no complaints. Except for an attack of serum sickness which lasted several days, the child became progressively better. The rigidity of the neck, as well as the other positive neurologic signs, disappeared, and she was discharged twenty-four days after admission, apparently well.

TUBERCULOUS MENINGITIS: STATISTICS OF COOK COUNTY HOSPITAL FOR 1933. DR. PHILIP L. ARIES.

There were 74 patients with tuberculous meningitis in the hospital in 1933. Forty-eight of these were children. During the same year there were 59 patients with suppurative nonmeningococcic meningitis and 260 with meningococcic meningitis. Of the children afflicted with tuberculous meningitis, 66 per cent were Negroes, 20 per cent were white and 14 per cent were Mexican. Fifteen children were under 2 years of age, fourteen from 2 to 5 years, eight from 5 to 7 years, five from 7 to 10 years and three from 10 to 12 years. During the first nine months of the year an average of 1 child was admitted each week. During the last three months of the year, however, only 4 patients with this condition entered the Children's hospital.

Measles and whooping cough were not important etiologic factors in this series. The history of a cold coming on from one to six weeks before the onset of meningitis was common. Severe trauma to the head seemed to be the predisposing factor in 1 infant.

The onset of the disease was usually insidious in a child who had been in good health and who was frequently well nourished. As a rule, the children entered the hospital on from the seventh to the fourteenth day of illness. The outstanding symptoms were occasional vomiting, fever, headache and listlessness. There was marked variation in the neurologic findings. The mentality remained clear until the last stages of the disease. The presence of a bulging fontanel in an infant aided in the diagnosis.

Physical and roentgen examination of the lungs gave variable results and often did not reveal pathologic conditions. The spinal fluid was usually typically changed. A low sugar content and a positive Levinson test are of significance. Spontaneously coagulating xanthochromic spinal fluid and a preponderance of polymorphonuclear cells were each observed once. The reaction to tuberculin was ordinarily positive, but a negative reaction does not exclude the disease. The leukocytes varied in number from 10,000 to 20,000, with a predominance of neutrophils. Leukopenia was reported in a few instances.

The duration of the disease from the onset of symptoms until death was most frequently from seventeen to twenty-one days, with variations of from eleven days to eight weeks. Tuberculous meningitis caused 7.6 per cent of the total number of deaths in the Children's Hospital unit.

POSTANGINAL SEPSIS. DR. ARCHIBALD HOYNE.

Recently, particular attention has been directed to postanginal sepsis. This condition was entirely new to me, but within the last month I have seen two cases. The results were the same: both patients died. In one of the children intubation was done after death, and the diagnosis was considered at that time. The situation was different from that in most instances in which there is dyspnea and severe infection, for the conditions which one expects to find were absent.

Both children were 3 years old, and they were ill for about five days. The temperature was 104.6 F. in one case and approximately that in the other. Because of the dyspnea, it was thought that there was some obstruction in the larynx or the trachea. There was no evidence of peritonsillar or retropharyngeal abscess. There was no edema of the epiglottis and there was only a slight degree of edema of the glottis, yet to all appearances the children needed intubation. Pressure on the muscles of the neck caused the throat to fill with pus; it was shown at necropsy that there was no abscess formation below the level of the trachea. The condition is not common. Possibly it follows tonsillitis, the infection traveling deep into the muscles of the neck.

I think that the proper treatment is to open the neck externally, but I have not seen any patient treated in this way. Probably if one watches for this condition one will find it more frequently.

MORBIDITY IN NEW-BORN INFANTS DELIVERED BY CESAREAN SECTION. DR. MAXWELL P. BOROVSKY.

During 1933, seventy-four cesarean sections were performed at the Cook County Hospital. The etiologic factors were mainly placenta praevia, premature separation of the placenta, preeclamptic toxemia and eclampsia.

Most of the babies of a gestation of seven months or more survived, and if proper care was administered, particularly to those born prematurely, there was no difficulty. We were especially interested in a group born at or near term, who had symptoms referable to some intracranial disturbance after cesarean section.

The following abnormal conditions were present:

CASE 1.—The mother, a colored woman, was a primipara and tertigravida. She had had one previous cesarean section. Pelvic disproportion and hypertension existed, but there was no toxic condition. The mother was not in labor when the section was performed.

The infant was delivered at full term and weighed 6 pounds and 4 ounces (2,835 Gm.). The cry was whining. The respirations were irregular. There were cyanosis of the hands and feet and tremor of the upper and lower extremities (+++).

On the second day cisternal puncture revealed a clear xanthochromic spinal fluid under increased pressure. The condition gradually cleared up.

CASE 2.—The mother was a 19 year old white primipara, in whom a mild degree of premature separation of the placenta was diagnosed. She was at term but not in labor. The baby was delivered with the aid of forceps. The weight at birth was 6 pounds and 12 ounces (3,061.8 Gm.). The baby was normal until the fifth day, when it suddenly became somnolent and then passed into a semicomatose state. There were spasms of the right arm and leg and right side of the face. Chvostek's sign was present. Moro's reaction was feeble and incomplete. At times nystagmus was noted. The respirations were shallow and irregular. Cyanosis and generalized convulsions followed. The clotting time of the blood was three and a half minutes. Intracranial injury was diagnosed. Human blood serum was given intramuscularly; 100 cc. of physiologic solution of sodium chloride was given by hypodermoclysis. The temperature rose to 103 F. The baby recovered after twenty-four hours.

CASE 3.—A 21 year old obese colored primipara came into the hospital at term in an eclamptic state. The blood pressure was 180 systolic and 108 diastolic. The urine contained albumin (4+) and many cells and casts. After five hours of preoperative treatment cesarean section was performed.

The baby weighed 6 pounds (2,721.5 Gm.) at birth. On the first day it was cyanotic; the respirations were labored, and the cry was feeble. Mucus accumulated in the throat, and coarse râles were heard throughout the chest. The urea nitrogen of the mother before operation was 17.25 mg. per hundred cubic centimeters; the uric acid, 6 mg.

On the first day the blood of the baby had 18 mg. of urea nitrogen and 7.5 mg. of uric acid per hundred cubic centimeters. On the fourth day the urea nitrogen was 14 and the uric acid 8.1 mg.

The mother recovered, and the child improved rapidly after twenty-four hours.

CASE 4.—A 23 year old colored woman had a normal pregnancy to term. She had a contracted pelvis, because of which cesarean section had been performed previously. The patient was not in labor when the section was performed. A 7½ pound (3,402 Gm.) infant was delivered. It was apparently normal at birth. Seven hours later, it became pale, and the cry was whining. The infant did not respond to stimulants (caffeine sodium benzoate and inhalations of a mixture of oxygen and carbon dioxide), but died promptly.

The diagnosis at necropsy was: cerebral hemorrhage due to trauma at birth. There were partial atelectasis of both lungs and patent foramen ovale.

CASE 5.—M. H., aged 36, an octipara who had had eleven pregnancies, entered the hospital with a condition diagnosed as preeclamptic toxemia. The blood

pressure was 248 systolic and 174 diastolic. She had had headache and dim vision. The urine contained albumin (4+) and granular and tubular casts. The blood urea nitrogen was 27.5, creatinine 1.9, sugar 79 and uric acid 6 mg. per hundred cubic centimeters. She was at term but not in labor when Porro cesarean section was performed. An infant weighing 5 pounds and 10 ounces (2,551.5 Gm.) was delivered. A few hours after birth the infant died with symptoms of intracranial hemorrhage. The mother's Wassermann reaction was negative, and roentgenographic examination of the bones of the baby revealed no pathologic changes.

CASE 6.—Cesarian section was performed during the seventh month of pregnancy because of a placenta praevia centralis in a woman who was a sexipara. The child died seven hours after birth.

CASE 7.—Porro's cesarean section was performed during the seventh month of pregnancy because of placenta praevia and hypertension in a white woman who had borne ten children and was pregnant for the thirteenth time. The baby died three hours after delivery. The mother died of postoperative paralytic ileus.

CASE 8.—A 23 year old colored woman, a unipara and secundigravida, entered the hospital during the eighth month of pregnancy because of a deformed pelvis and because she had had a previous cesarean section. She remained under observation in the hospital for a month, until the full term of pregnancy was reached. The blood pressure was normal. The Wassermann reaction was negative. The patient was not in labor when cesarean section was performed.

The baby weighed 3 pounds and 14½ ounces (1,771.8 Gm.) at birth. It was weak and cyanotic. The respirations were labored. The infant died after seven hours.

CASE 9.—Porro's cesarean section was performed on a white woman, a tertipara and quadrigravida, because of previous difficult labors due to a rigid cervix. The blood pressure was 152 systolic and 80 diastolic. A 7½ month premature infant weighing 4 pounds and 7 ounces (2,012.8 Gm.) was delivered. The cry was weak and listless. There were a purpuric eruption on the forehead and arms and ecchymoses into the soles. A tremor designated as ++ was present. The coagulation time of the blood was six minutes and forty-five seconds. Forty-five cc. of human blood serum was injected intramuscularly. The infant recovered and left the hospital within seven weeks, weighing 6 pounds and 8 ounces (2,948.3 Gm.).

CASE 10.—A 38 year old colored woman, a septipara who had had eleven pregnancies, came to the hospital bleeding from a placenta praevia lateralis after a gestation period of seven and one-half months. A low cervical Porro cesarean section was performed, and twins were delivered. One weighed 3 pounds and 8 ounces (1,587.6 Gm.) at birth, and the other 3 pounds and 2 ounces (1,417.5 Gm.). On the second day there were extensive hemorrhages into the muscles and skin of the extremities in both cases and into the abdominal wall in one case. Hemorrhagic disease of the new-born was diagnosed. The twins recovered rapidly after human serum was injected intramuscularly.

One baby left the hospital in good condition after two months, weighing 6 pounds (2,721.5 Gm.). The second baby contracted bronchopneumonia when it was 5 weeks old and died within twelve hours after the onset.

The conclusions that I wish to draw from these observations are simply that delivery by cesarean section does not preclude the possibility of intracranial pathologic conditions in the new-born.

In five of these cases there was definite evidence of an intracranial pathologic condition. In some instances toxemia or hemorrhagic disease of the new-born could be accepted as the etiologic factor, but these were not present in all the patients.

Sudden changes of atmospheric pressure and trauma from the use of forceps at the abdominal delivery must be considered as possible causes of intracranial lesions.

AGENESIS ABDOMINALIS. DR. ARTHUR H. PARMELEE.

This infant was born normally at Cook County Hospital on Oct. 4, 1933; it weighed 8 pounds and 4 ounces (3,742.1 Gm.) and was in good condition at birth. The abdomen was large and lax, and the wall was soft and doughy; the outline of the abdominal muscles could not be made out, and there was no tone to the abdominal wall, even in the flanks. There were deep wrinkles in the skin, and the whole picture was that of the abdomen of a woman who had just been delivered of a child. The abdominal viscera could be easily palpated. All the other findings were normal. The weight dropped to 7 pounds (3,175.1 Gm.) at the end of the first week, but the child did not seem ill.

Roentgenograms were negative for lesions of osseous syphilis.

The mother was 21 years old. This was her third pregnancy. She had had two premature infants (7 months) who did not live.

The Wassermann and the Kahn reaction of the blood were negative.

Three weeks after discharge from the hospital the child died. The cause of death was not known.

THE TREATMENT OF TETANUS. DR. R. SPAETH.

As a result of the high mortality in cases of tetanus in the University of Iowa City Hospital, a study was undertaken in which it was found that convulsions, in the absence of other causes to account for death, constituted the most frequent basis for a fatal outcome. In practically all the cases of convulsions death resulted from asphyxial spasms of the respiratory musculature. Among ten patients with convulsions the mortality was 70 per cent, whereas among eighteen without obvious muscle spasms there was only one death—in a patient, aged 65, from lobar pneumonia.

As a result of animal experimentation, confirmed by subsequent clinical experience, a new treatment was established in the children's division of the University Hospital. The outline is essentially as follows:

1. Convulsions are immediately controlled with avertin fluid (tribromethanol amylene hydrate) by giving an enema containing 50 mg. per kilogram of body weight, and using minimal additional amounts after about five minutes to induce and maintain a state of moderate relaxation and freedom from tonic convulsions. The avertin fluid is given over prolonged periods. Bromeis at Tübingen used it for twenty-eight days in a 9 year old patient, with final recovery.

2. Antitoxin is injected intravenously in several hundred cubic centimeters of physiologic solution of sodium chloride. A single dose of 60,000 units is given in cases with a one week period of incubation, and from 100,000 to 200,000 units in cases with shorter periods of incubation. Subsequent injections are not given, since it has been demonstrated by titrations on animals in six different cases that the level of antitoxin in the blood is high for as long as thirty days after the intravenous administration of only 60,000 units. The intrathecal route is rigidly forbidden because of the danger of serum meningitis with consequent convulsions in already excitable patients, the hazard of sudden respiratory failure and the efficacy of the intravenous route alone, as has been demonstrated by animal experimentation and clinical observation in our own six patients and in those of other clinicians, namely, Freedlander at Cleveland City Hospital and Silverthorne and Hart at the Hospital for Sick Children, Toronto.

3. Surgical intervention is not considered an emergency measure and is not instituted until effective treatment with sedatives and antitoxins has been carried out. A conservative program is followed, and only such surgical measures are employed as would be undertaken in the absence of tetanus. Amputation is generally avoided, since antitoxin circulating in the blood stream results in the neutralization of the toxin being formed at the local focus.

4. Nursing care and medical treatment consist of the following measures: immediate access to a medical attendant to control convulsions with avertin fluid; twenty-four hour individual nursing attention to detect immediately the onset of

asphyxial spasms; maintenance of an adequate intake of fluid by nipple and bottle or by a medicine dropper or nasal catheter; frequent aspiration of the nasopharynx to prevent pneumonia from aspiration of mucus; frequent sponge baths and changes of position in bed as prophylaxis against convulsions and pneumonia, and careful control of the serum reaction by frequent injections of epinephrine hydrochloride, mentholated and phenolized calamine lotion and adequate amounts of avertin fluid. Observation of fatal outcomes in the absence of the general measures just mentioned serves to emphasize the fundamentally important rôle of these procedures in rendering effective the other features of the program for the treatment of tetanus.

Six consecutive patients with tetanus have been treated successfully in the children's division of the University Hospital by the foregoing routine, one patient requiring fairly large doses of avertin fluid for ten days. The table serves to show

*Influence of Avertin on Mortality in Tetanus*

| | No Serum | | Serum Alone | | Serum with Avertin | |
|---|---|---|---|---|---|---|
| Incubation Period | Cases | Deaths, per Cent | Cases | Deaths, per Cent | Cases | Deaths, per Cent |
| 10 days and under..... | 325 | 95.4 | 731 | 73.6 | 35 | 34.3 |
| Over 10 days..... | 235 | 68.5 | 568 | 38.5 | 13 | 23.0 |

the influence of avertin fluid, with the other parts of the treatment as variables, on the mortality in tetanus; it includes all cases cited in the available literature.

The causes of death in patients treated with avertin fluid were: pneumonia, in six; sepsis, in three, and asphyxia, in one. In five cases the cause was not stated. By using minimal amounts of avertin fluid and by the institution of assiduous and skilful nursing care, the incidence of pneumonia, it is believed, will be appreciably lessened.

## NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS AND SECTION OF OBSTETRICS AND GYNECOLOGY

*Combined Meeting, March 8, 1934*

MARTHA WOLLSTEIN, M.D., *Presiding*

MORPHINISM IN THE NEW-BORN: REPORT OF A CASE. DR. R. GORDON DOUGLAS.

DISCUSSION

DR. RICHARD N. PIERSON: At the Sloane Hospital for Women from 1919 to the present there has been in the obstetric service only one case of parturition in a morphine addict. The clinical history is as follows: This patient, a white primipara, aged 28, was sent to the hospital as an emergency patient on May 8, 1928. At the time of admission, the blood pressure was 160 systolic and 90 diastolic, and urinalysis showed albumin (80 per cent by volume).

She had had severe asthma since childhood. A few months before admission a physician gave her medicine for her asthmatic attacks, and this medicine contained morphine. She acquired the morphine habit, and at the time of admission had been taking 1.5 Gm. daily.

The patient was in labor at the time of admission and after seven hours was delivered normally of a girl weighing 3 pounds and 8 ounces (1,587.5 Gm.), who showed no signs of asphyxia and was in good condition. The pathologic report was that the placenta, cord and membranes were normal. General physical exam-

ination of the patient during labor showed essentially normal conditions save for a hypodermic abscess on the right thigh. Ten hours after delivery the patient showed marked symptoms of withdrawal of morphine, anxiety, pronounced muscular twitching and profuse perspiration, and begged for morphine. She was kept on morphine, 1 Gm. daily, for the first ten days. She was also given large doses of bromides and chloral. On May 25, the seventeenth day post partum, the narcosan withdrawal treatment was started. This consisted of 1 cc. of narcosan every four hours for two days, and then 1 cc. every six hours until the transference of the patient to Bellevue Hospital on June 2. She was transferred to Bellevue Hospital because she had become unmanageable and at times irrational. She remained in that hospital for one week and was then discharged in good condition. She was seen in the follow-up clinic at the Sloane Hospital for Women on June 14, at which time she was physically well and said that she had no desire for morphine. She was referred to the medical clinic because of her asthma.

The baby did not nurse at the mother's breast at any time. Except for a temperature of 102 F. on the third and fourth days, she seemed clinically normal until the seventh day, at which time she became restless and had an extremely rapid respiratory rate and a temperature of 106 F. She was given 0.001 Gm. of morphine twice within twelve hours, after which her clinical condition appeared to be normal, with a satisfactory gain in weight up to the time of discharge. She weighed 4 pounds and 7½ ounces (2,026.9 Gm.) on the twenty-fifth day. The baby died in Bellevue Hospital, but the cause of death could not be discovered.

These two cases demonstrate certain facts and suggest some questions in respect to drug addiction which have not been completely answered. In the first place, the cases show beyond any question that morphine passes through the placental circulation and may affect the baby. Some obstetricians deny this because in certain instances morphine has not been found in the bodies of new-born babies who were thought to have died because of respiratory depression brought about by the mothers having received morphine during labor.

These cases emphasize the great danger of giving morphine to a patient for any chronic condition. In both cases the condition for which the drug was given was chronic bronchial asthma. Dr. Alexander Lambert, who discussed the problem with me recently, said that there is danger of otherwise normal people becoming addicted to morphine from using the drug for as long as three weeks, and that a much shorter period might cause addiction to the drug in a psychopathic person. He explained the present theory that the symptoms of withdrawal are allergic phenomena. That is why, in the new treatment of morphinism with rossium, the symptoms of withdrawal are dramatically relieved by small doses of epinephrine hydrochloride.

Dr. Lambert pointed out that the habitual use of barbital or of hypnotics similar to it frequently offers a more difficult therapeutic problem than morphinism. Clinical obstetricians should bear this in mind in their perhaps too zealous use of these drugs during pregnancy, labor and puerperium.

GAS THERAPY IN OBSTETRICS AND PEDIATRICS. DR. PALUEL J. FLAGG.

Should a pregnant woman in the hospital suffer from an overdose of an opiate to the point where respiration is gradually failing and death impends; should a patient, in the course of a forceps operation, suddenly vomit and aspirate the contents of her stomach; should a child, while playing with his toys in the ward, suddenly aspirate a foreign body into his pharynx, obstructing respiration; should a patient suddenly become cyanosed and dyspneic following tonsillectomy; should a new-born baby fail to breathe or a 3 day old infant become progressively cyanosed—what member of the staff is constantly available, trained and equipped to meet the emergency intelligently and to render advice as to the subsequent care?

These and many other questions relating to the personnel and the equipment of the modern hospital will bring out in sharp relief the unpreparedness of the average institution to meet asphyxial emergencies.

The rapidly increasing use of gases for saving life, controlling pain and treating disease suggests the necessity of coordinating the activities of those interested in the use of gases for the purpose of providing a well trained personnel and adequate equipment. It is only by such organization that a sequence of instruction may be provided and records of value secured.

The hospital department of gas therapy should provide skilled medical care in asphyxial accidents. It should direct the routine use of gases and vapors for inhalation anesthesia, as well as the oxygen therapy commonly used for acute conditions of the respiratory tract.

Most well organized institutions possess a department of anesthesia the functioning of which is a routine activity of the hospital. Some institutions, because of the interest of a particular internist on the staff, are also equipped to provide oxygen therapy. A few institutions which have received instruction in modern methods of medical resuscitation are successfully coping with their acute asphyxial emergencies. It is safe to say, however, that at present there is no institution in which these three departments (naturally correlated because their work depends on the employment of gases) are well organized and integrated to function as a single department. The need of such integration is obvious to any one familiar with the accidents and routine requirements of a general hospital service. The need is even more urgent in the small suburban institution than in the large medical center because of the infrequency with which such accidents occur there and the consequent lack of preparation for care of the patients involved.

The minimum personnel of such a department should consist of a physician qualified in gas therapy in its three branches and under him two resident physicians who should be on call to provide a continuous coverage for the emergencies. Technicians in the administration of anesthetics and other specialists may be added to this group, as required.

Material for instruction in the practice of modern methods of medical resuscitation is continuously available through the anesthetic department, in which the unconscious, anesthetized patient resembles in almost every particular the unconscious, asphyxiated patient who is to be relieved from the threat of impending death.

Asphyxia neonatorum is a condition which may be anticipated and which may be treated with the greatest hope of success. The technic of treatment for asphyxia should, therefore, be developed from this point. Once the principles of the technic in this condition are grasped, variations necessary in the treatment of adults may readily be acquired. For the details of modern methods of medical resuscitation, reference may be made to my bibliography on this subject.

DISCUSSION

DR. RICHARD N. PIERSON: All obstetricians are indebted to Dr. Flagg for his untiring efforts to teach them how to resuscitate asphyxiated babies better. He would be the first to agree that the obstetrician's primary responsibility is to use such judgment during labor and at the time of delivery that babies are not asphyxiated at birth. This brings up the whole question of analgesia and anesthesia in obstetrics. Some happy medium between the extremists who believe in little or no anesthesia and those who strive for complete amnesia seems to be desirable.

There will always be, however, an occasional injured or asphyxiated baby. For a baby without muscle tone and without laryngeal reflexes, Dr. Flagg's apparatus will, in certain cases, be a life saver. In babies with active reflexes the shock of intubation may have disastrous results.

I am sure that all the members wish Dr. Flagg every success in his campaign of educating the medical profession to the need of the well trained gas therapist.

NATIMORTALITY. DR. HUGO EHRENFEST, St. Louis.

Obstetricians must regard as a failure in the reproductive process every pregnancy which does not end in the birth of a live and viable child. This loss of

expected offspring represents a mortality during the course of the natal process and thus appropriately can be expressed by the term "natimortality." This word designates compactly what one commonly is forced to describe by the cumbersome term "fetal, intranatal and neonatal mortality." It is not surprising that information concerning the extent of natimortality is extremely meager, since such statistics obviously have to include the loss of fetal lives through both criminal and spontaneous abortions. However, Rothert's exhaustive study, "Maternal Mortality in Fifteen States," incidentally reveals the surprising fact that even with the exclusion of neonatal mortality the loss of life amounts to at least 57 per cent.

All available statistics indicate that in relative importance for natimortality, abortion probably ranks first, followed by stillbirth and, closely after, by neonatal death.

Among the factors chiefly accounting for a steady increase in criminal abortions are: (1) an increase of surviving children as a result of the marked decrease in infant mortality; (2) the present economic distress and (3) the changed social position of woman. To mitigate the potent influence of economic distress falls outside the domain of medical effort. There can be no desire to halt the continuous fall in infant mortality. Obstetricians necessarily are interested in the question of the limitation of offspring. It seems that the newly granted right of woman to determine the size of her family by the use of contraceptive measures not rarely leads her to the fallacious conclusion that she is entitled to an abortion if contraceptives have failed. Physicians should never give contraceptive advice without the warning that no absolutely reliable method is known to the medical profession. The laity is far from appreciating the great dangers of criminal abortion. In many instances a sympathetic physician, particularly if aided by a competent social worker, can persuade a woman to refrain from contemplated interruption of pregnancy.

A considerable percentage of all spontaneous abortions are caused by disease, pelvic anomalies, overexertion, improper diet and other factors which can be discovered at the first thorough antepartum examination or in the course of adequate antepartum care. Prepartum supervision, started early in pregnancy, undeniably saves not only many maternal lives, but many fetal lives as well. Such supervision also admittedly reduces the number of required therapeutic abortions.

During 1928, 89,765 stillbirths and 83,068 deaths within the first month of life were reported from the birth registration area. In regard to these two large portions of total natimortality the following pertinent statements can be made: Unfortunately, official vital statistics do not permit the division of stillborn infants into two definite groups, namely, those dead before labor started and those dying during labor. The factors causing death in the first group are, in general, the same which result in abortion before the twenty-eighth week of gestation. Including the late toxemias and excluding only placental anomalies, they are mitigated or eliminated if the mother is under prepartum care. Conditions are entirely different for the second group, which represents an obstetric problem. Here the causes of death are, to a large extent, the same as those responsible for the death of infants within the first few days of life. Among these causes the most prominent are trauma at birth, asphyxia and prematurity. These three etiologic factors, however, stand in close relation to each other. Available statistics indicate that about one third of all deaths during the first month occur on the first day. It can be roughly calculated that, of 100 viable dead new-born infants, 36 died before labor started, 26 during labor and the remaining 38 within the first few weeks of life. It is this great loss during and soon after labor that concerns obstetricians, and autopsies have established, beyond any possible doubt, that traumatization of some sort is the most important etiologic factor. One is forced to the conclusion that a most urgent problem of practical obstetrics is the prevention, so far as is possible, of any type of traumatization of the child during birth.

DISCUSSION

DR. WILLIAM E. STUDDIFORD: The term "natimortality," if it is restricted to the total loss of viable fetuses and new-born infants occurring ante partum, intra partum or post partum, is an advisable one. The inclusion under this term of pregnancies terminated by abortion is unfortunate. Many abortions of the spontaneous variety are secondary to death and degeneration of the ovum and are in no way preventable. Many aborted fetuses are reported to present anomalies, and in such cases it is fortunate that abortion occurs. Abortions which are classified as therapeutic or criminal are performed, on the one hand, because of medical indications and, on the other, for social, economic or purely selfish reasons of the mother. Such abortions constitute wilful killing of the fetus on the part of the physician or the abortionist and should not concern one in a consideration of natimortality. The inclusion of abortions only serves to confuse.

The investigation of fetal deaths occurring in the period of viability is of great importance. It can be accomplished only by complete autopsies and correlation of the clinical facts. In any such series of autopsies the importance of trauma and prematurity will stand out. During the past year about 2,000 women have been delivered of their infants at Bellevue Hospital. Twenty per cent of these, or about 400, were delivered prematurely. During the same time there was a loss of approximately 160 fetuses and new-born infants. About 80 per cent, or 137 of these infants, came to autopsy. Of these, 97 were born before the thirty-eighth week and 40 were born at term. The natimortality in the premature infants, therefore, was about from 25 to 30 per cent; that of the infants born at term was 3 per cent. Of the 97 premature infants, 24 showed traumatic lesions. None was delivered with instruments, and 4 were born with breech presentation. Of the 40 infants born at term, 11 showed traumatic lesions. Four of these were delivered with forceps, 2 were born with breech presentation and 2 with version and breech presentation. The remaining 3 were delivered spontaneously. It can therefore be seen that prematurity is a tremendous factor in this mortality. While in many of these cases there was an obvious exciting cause for premature labor, in a large group there was not. An exact knowledge of the cause of labor and the means of preventing premature labor would lead to an enormous reduction in mortality. Finally, it is well to bear in mind that premature infants do not stand the forces of normal labor well because of their lack of development. Might not many viable premature infants be saved by gentle forceps extraction and episiotomy in the second stage?

DR. F. A. HEMSATH: With reference to Dr. Ehrenfest's rather remarkable figures of 7,226 pregnancies with only 51 per cent resulting in the birth of live children, I wish to present the figures for 8,835 consecutive confinements in the New York Lying-in Hospital from November 1929 to November 1931. Ninety-two and nine-tenths per cent resulted in the birth of children who were discharged as healthy on the tenth day. The other 7.1 per cent were divided as follows: stillborn infants weighing more than 1,500 Gm., 1.27 per cent; dying new-born infants weighing more than 1,500 Gm., 1.34 per cent; macerated stillborn infants weighing more than 1,500 Gm., 1.08 per cent; stillborn premature infants and dying premature infants weighing from 1,000 to 1,500 Gm., 3.23 per cent; aborted fetuses weighing less than 1,000 Gm., 0.66 per cent, and infants with congenital deformities incompatible with life, 0.52 per cent.

I believe that, since the human organism is imperfect, mortality is inevitable during the nine months following the fertilization of the ovum as surely as during the nine months following birth, in a certain number of cases. With respect to the mature fetus, the prevention of its death is intimately associated with the treatment of syphilis and the prevention of other intra-uterine infections, with the prevention and treatment of toxemia and with the management of labor in presentations other than the occiput anterior and in complications of labor, such as placentia praevia, prolapsed cord and relative disproportion.

Dr. Ehrenfest has diplomatically used the term "birth trauma" without unduly stressing the trauma of operative delivery. In the presence of disproportion, trauma is frequently inevitable, whether the fetus is delivered by forceful spontaneous uterine contractions or by operative methods. Most of the types of injury at birth occurring in operative delivery, viz., lacerations of the tentorium, subdural hemorrhage and fractures of the cranial vault and base of the skull, have been found at autopsy in spontaneous deliveries. Complete autopsies by competent pathologists will frequently show injury at birth and thus decrease the percentage of deaths otherwise assigned to asphyxia neonatorum. The interpretation of observations at autopsy is complicated when injuries are found together with the signs of asphyxia (cardiac dilatation, cerebral congestion and petechial hemorrhages of the pleura, pericardium and thymus). With other workers, I have been inclined to minimize the asphyxia and stress the injury. J. N. Cruickshank, on the other hand, in his review of 800 autopsies in cases of neonatal death, considered asphyxia the primary cause of death in 68 per cent of the series.

# Book Reviews

**Die Geburtsverletzungen des Kindes.** By Prof. Dr. Med. Hans Naujoks. Price, 50 marks. Pp. 132, with 49 illustrations. Stuttgart: Ferdinand Enke, 1934.

This small book on the injuries of the new-born infant sustained at birth is written by an obstetrician. It is a valuable contribution to medical literature, because this important subject is discussed from the standpoint of the one group of medical practitioners who are in a better position than any other to reduce the high infant mortality of the new-born period. The subject matter is divided into two chapters. In the first the author deals with the origin of injuries at birth and discusses measures that obstetricans may use to prevent them; in the second he describes the clinical manifestations of the various injuries and discusses methods of treatment.

The subject is handled in a systematic and exhaustive manner by a clinician of wide experience. The author has not, however, made use solely of his own clinical material, but has had access to that of his colleagues in many of the large obstetric clinics of Germany. The relative importance of the various injuries has been properly recognized, and an appropriate amount of space has been given to them. The subject of intracranial birth injuries, for example, is allotted sixteen pages. The sane and fair-minded manner in which the author has treated various theoretical considerations and different methods of therapy adds greatly to the value of the book, because the conclusions are thereby made more convincing to the reader.

The book is well written and has many excellent illustrations. It deserves to be widely read by obstetricians and pediatricians alike.

**Traité de médecine des enfants. Volume V.** By P. Nobécourt and L. Babonneix. Paper. Unbound, 150 francs; bound, 170 francs. Pp. 900, with illustrations. Paris: Masson & Cie, 1934.

This fifth and last volume of the French system of pediatrics, edited by Nobécourt and Babonneix, takes up, first, diseases of the nervous system and associated conditions, including those of the muscles. This part of the work is extensive and well done and is excellently and elaborately illustrated. This is followed by a section on therapeutics, the first part of which consists of prescriptions, many of which would be unintelligible to American readers. The rest of the therapy, however, is extensive in detail and broadly conceived, including climatotherapy and physical therapy. There is a chapter on insufficiency of the respiration and reeducation and also one on biologic medication. The whole volume is in line with the other four and is very complete. This is followed by an index for the five volumes.

**New Patterns in Sex Teaching.** By Frances Bruce Strain. Price, $2. Pp. 176. New York: D. Appleton-Century Company, 1934.

This book is intended to be a general guide to sex education for children. The point of view is that generally accepted in mental hygiene. It is written in an easily understandable manner. The terminology is not too difficult for the laity. Sex is described as a primary emotional impulse. It is discussed from birth through adolescence. The everyday problems met at various levels of development are discussed. There is emphasis on sex questions that arise in handling children. The material was gathered from many years of observation and experience with children. The book is interesting, concise and scientific. While the conclusion and general principles are not new, the method of approach to the problem is interesting, practical and thorough.

**Hygiène et alimentation du nourrisson.** By G. Paisseau. Price, 12 francs. Pp. 86. Paris: Gaston Doin & Cie, 1934.

This monograph deals with the care and feeding of infants chiefly. It seems to have been written for nurses, social service workers and laymen rather than for physicians, as the topics are discussed in an elementary manner. In the first chapter prenatal hygiene is discussed. This includes the marriage of narcotic addicts and the prevention of tuberculosis and syphilis. The measures adopted in France for medical and social care during pregnancy are described. The physiology and hygiene of the new-born period are rather briefly considered. The directions for the feeding of infants are more extensive. The final chapter contains a discussion of procedures of value in preventing common contagious and infectious diseases during infancy.

**Sex in Childhood.** By E. R. Groves and G. H. Groves. Price, $3. Pp. 247. New York: Macaulay Company, 1934.

There is nothing in this book that has not been said before and much that had been better left unsaid. If it had been reduced to about one-third its size and if a sharper differentiation had been made between fact and fancy, it would have more merit. There is considerable padding of rather pointless letters from mothers. Even if the book were one to be recommended by the physician to parents, which the reviewer believes that it is not, the undignified jacket cover, apparently designed to catch the eye of the reader of the "pulp magazine" on the news-stand, would cause him to hesitate. The reviewer thinks that the education of parents and youth in matters of sex is not materially aided by this volume.

**Die Wiener Diphtherie-Endemic der letzten Jahre.** By Dr. Hermann Zischinsky. Price, 9.60 marks. Pp. 170. Berlin: S. Karger, 1934.

Previous to 1926, the type of diphtheria seen in Vienna was mild, but since that year there has been a great deal of severe diphtheria, with numerous complications and high fatality. The author reports his clinical observation of numerous cases of malignant diphtheria. The clinical course, pathology and complications are discussed extensively. The epidemiology, prophylaxis and treatment are also considered. Comparison is made with milder forms of diphtheria seen in other years. This is an interesting and informative presentation of the type of diphtheria seen in Vienna during the past few years.

# Directory of Pediatric Societies *

## INTERNATIONAL

### International Association of Preventive Pediatrics

President: Professor Taillens, Lausanne, Switzerland.
Secretary: Dr. P. Oltramare, rue Decandolle, Geneva, Switzerland.

## FOREIGN

### Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. Leonard G. Parsons, 58, Calthorpe Road, Birmingham, England.
Secretary: Dr. W. G. Wyllie, 33, Wimpole St., W. 1, London.

## NATIONAL

### American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. A. Graeme Mitchell, Children's Hospital, Cincinnati.
Secretary: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Place: Atlantic City, N. J. Time: June 10-14, 1935.

### American Academy of Pediatrics

President: Dr. John Ruhräh, 11 E. Chase St., Baltimore.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.

### American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st., New York.

### American Hospital Association, Children's Hospital Section

President: Mr. Robert Witham, Children's Hospital, Denver.
Secretary: Miss Agnes O'Roke, Kosair Crippled Children's Hospital, Louisville, Ky.
Place: Philadelphia. Time: Sept. 24-28, 1934.

### American Pediatric Society

President: Dr. Borden S. Veeder, 3720 Washington Ave., St. Louis.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.

### Canadian Society for the Study of Diseases of Children

President: Dr. D. P. Arnold, 159 Bidwell Parkway, Buffalo, N. Y.
Secretary-Treasurer: Dr. R. R. Struthers, 1414 Drummond St., Montreal.
Place: Buffalo, N. Y. Time: June 1935.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

### Society of Pediatric Research

President: Dr. Joseph Stokes Jr., Children's Hospital, Philadelphia.
Secretary: Dr. A. A. Weech, Babies Hospital, New York.
Place: Atlantic City, N. J. Time: May 1935.

## SECTIONAL

### North Pacific Pediatric Society

President: Dr. Arthur H. Gray, 1117 Second Ave., Seattle.
Secretary: Dr. Raymond H. Somers, Cobb Bldg., Seattle.

### Southern Medical Association, Section on Pediatrics

Chairman: Dr. Oliver W. Hill, 511 W. Church St., Knoxville, Tenn.
Secretary: Dr. Madison Hines Roberts, 104 Ponce de Leon Ave., N. E., Atlanta, Ga.

## STATE

### Alabama Pediatric Society

President: Dr. C. E. R. Parker, 401 S. Court St., Montgomery.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22d St., Birmingham.

### Georgia Pediatric Society

President: Dr. Benjamin Bashinski, 700 Spring St., Macon.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Atlanta. Time: Oct. 25, 1934; May 1935.

### Louisiana State Pediatric Society

President: Dr. John Signorelli, Louisiana State University Medical School, New Orleans.
Secretary-Treasurer: Dr. Edwin A. Socola, Louisiana State University Medical School, New Orleans.
Place: New Orleans. Time: April 1935.

### Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Adolph G. De Sanctis, 12 E. 11th St., New York.
Secretary: Dr. George M. Retan, 459 James St., Syracuse.

### Michigan State Medical Society, Pediatric Section

Chairman: Dr. W. A. Collins, 103 W. Burdick St., Kalamazoo.
Secretary: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Place: Battle Creek. Time: Sept. 12-14, 1934.

### Mississippi State Pediatric Society

President: Dr. N. C. Womack, Jackson Infirmary, Jackson.
Secretary-Treasurer: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Place: To be designated by Society. Time: Yearly.

### Nebraska Pediatric Society

President: Dr. W. O. Colburn, 725 Sharp Bldg., Lincoln.
Secretary-Treasurer: Dr. C. G. Weigand, 1614 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

### North Carolina Pediatric Society

President: Dr. J. Buren Sidbury, 15 N. Fifth St., Wilmington.
Secretary: Dr. E. K. McLean, 121 W. Seventh St., Charlotte.
Place: Various children's hospitals. Time: Twice a year.

### Oklahoma State Pediatric Society

President: Dr. C. V. Rice, 222 Wall St., Muskogee.
Secretary: Dr. B. H. Nicholson, 301 N. W. Twelfth St., Oklahoma City.
Place: Oklahoma City. Time: May 1935.

### South Carolina Pediatric Society

President: Dr. Julian P. Price, Medical Bldg., Florence.
Secretary-Treasurer: Dr. Leland B. Salters, 317 S. Warley Ave., Florence.

### Tennessee State Pediatric Society

President: Dr. Arthur G. Jacobs, 1193 Madison Ave., Memphis.
Secretary: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.

### Texas Pediatric Society

President: Dr. Sidney R. Kaliski, Moore Bldg., San Antonio.
Secretary-Treasurer: Dr. Frank M. Martin, 321 Medical Arts Bldg., San Antonio.

### Virginia Pediatric Society

President: Dr. Thomas D. Jones, Medical Arts Bldg., Second and Franklin Streets, Richmond.
Secretary: Dr. W. A. McGee, 2618 Grove Ave., Richmond.
Place: Alexandria. Time: Oct. 9-11, 1934.

### West Virginia State Medical Society, Section on Pediatrics

President: Dr. R. C. Hood, 428 W. Pike St., Clarksburg.
Secretary: Dr. Russell C. Bond, 1325 Chapline St., Wheeling.

## LOCAL

### Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. A. Garvin, Carnegie Medical Bldg., Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

### Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Secretary: Dr. Lawrence Murray, 1870 Bloor St., W., Toronto.

### Bronx Pediatric Society

President: Dr. Morris Gleich, 9 Post Ave., New York.
Secretary: Dr. Harry D. Pasachoff, 1560 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

### Brooklyn Academy of Pediatrics

President: Dr. Carl H. Laws, 12 Pierrepont St., Brooklyn.
Secretary: John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

### Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

### Chicago Pediatric Society

President: Dr. Charles Schott, 48 W. Division St., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

### Dallas County Pediatric Society

President: Dr. P. E. Luecke, 4105 Live Oak St., Dallas, Texas.
Secretary: Dr. R. S. Usry, 1835 Garrett Ave., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

### Detroit Pediatric Society

President: Dr. John A. Johnston, 2799 W. Grand Blvd., Detroit.
Secretary: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month.

### Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. L. H. Muse, 384 Peachtree St., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

### Houston Pediatric Society

President: Dr. Frank Lancaster, Medical Arts Bldg., Houston, Texas.
Secretary-Treasurer: Dr. A. A. Little Jr., 817 Holman Ave., Houston, Texas.
Time: Third Monday of each month.

### Intermountain Pediatric Society

President: Dr. Helmina Jeidell, 11 Exchange Pl., Salt Lake City, Utah.
Secretary-Treasurer: Dr. Edwin R. Murphy, 9 Exchange Pl., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

### Kansas City (Missouri) Pediatric Society

President: Dr. Hugh L. Dwyer, 406 W. 34th St., Kansas City.
Secretary: Dr. John Aull, 906 Grand Ave., Kansas City.

### Medical Society of County of Kings and Academy of Medicine of Brooklyn

President: Dr. Harry M. Greenwald, 499 Ocean Ave., Brooklyn.
Secretary: Dr. Sylvan D. Lazarus, 847 Lincoln Place, Brooklyn.
Place: Medical Society of County of Kings Bldg., 1313 Bedford Ave., Brooklyn.
Time: Third Wednesday of aech month from October to May, 8:30 p .m.

### Memphis Pediatric Society

President: Dr. Harry J. Jacobson, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Clyde V. Croswell, 1052 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

### Milwaukee Pediatric Society

President: Dr. F. R. Janney, 1411 Wauwatosa Ave., Wauwatosa, Wis.
Secretary: Dr. John H. Reynolds, 1628 Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

### New England Pediatric Society

President: Dr. James L. Gamble, 33 Edgehill Road, Brookline, Mass.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Chairman: Dr. Martha Wollstein, Babies' Hospital of City of New York, New York.
Secretary: Dr. Harry Bakwin, 132 E. 71st St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. Alexander Stewart, 459 Lowry Medical Arts Bldg., St. Paul.
Secretary: Dr. E. F. Robb, 1801 Lyndale Ave., S. Minneapolis.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala, Pa.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. Henry C. Flood, 119 S. Highland Ave., Pittsburgh.
Secretary: Dr. E. R. McCluskey, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

RICHMOND PEDIATRIC SOCIETY

President: Dr. W. A. McGee, 2618 Grove Ave., Richmond, Va.
Secretary-Treasurer: Dr. Emily Gardner, 1100 W. Franklin St., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

ROCHESTER PEDIATRIC SOCIETY

President: Dr. H. F. Rowley, 176 S. Goodman St., Rochester, N. Y.
Secretary: Dr. J. M. Parker, 26 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month from October to May.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. Arthur L. Esserman, Republic Bldg., Denver.
Secretary: Dr. Ralph Verploeg, 19th and Gilpin Sts., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7 p. m.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Armin C. Rembe, 1215 4th Ave., Seattle.
Secretary: Dr. Frank H. Douglass, Medical-Dental Bldg., Seattle.
Place, College Club. Time. Third Friday of each month, 7 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Victor E. Stork, 1136 W. Sixth St., Los Angeles.
Secretary: Dr. Howard R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. John F. Sanders, 320 Townsend St., Lansing, Mich.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Place: University Hospital, Ann Arbor, Mich. Time: Nov. 23-24, 1934.